Archives of Neurology and Psychiatry

VOLUME 44 AUGUST 1940 NUMBER 2

COPYRIGHT, 1940, BY THE AMERICAN MEDICAL ASSOCIATION

PRIMARY CORTICAL CENTERS FOR MOVEMENTS OF UPPER AND LOWER LIMBS IN MAN

OBSERVATIONS BASED ON ELECTRICAL STIMULATION

JOHN E. SCARFF, M.D.

NEW YORK

It has been generally accepted for many years that in man, as in the apes, the cortical centers for primary movements of the toes, ankle, knee, hip, abdominal and thoracic muscles and the corresponding axial musculature are situated in the precentral gyrus on the lateral surface of the cerebral hemisphere. The center for the toes is usually assigned to a place at the superior margin of the hemisphere, extending somewhat over onto the mesial surface of the brain, while centers for other parts of the lower extremity and trunk are represented as occurring in the order named from above downward on the lateral convexity of the cerebrum [1] (fig. 1 *A*).

My own observations, however, made while stimulating the human brain at the operative table, suggest that in man the so-called motor cortex has "migrated" to a higher position on the lateral convexity of the hemisphere than it occupies in any of the other primates, so that, as a rule, the centers governing primary movements of the upper extremity extend quite up to the superior border of the hemisphere, whereas, in most instances, the lower extremity is entirely unrepresented on the lateral surface of the hemisphere (fig. 1 *B*).

Because of the obvious disparity between the generally accepted view and my own observations regarding the position of the primary "leg areas" of the human cortex, a critical review of the literature was undertaken to determine, so far as possible, the evidence on which these earlier concepts had gained acceptance.

From the Department of Neurology, Columbia University College of Physicians and Surgeons, and the Neurological Institute of New York.

Reported March 7, 1939, at a joint meeting of the New York Neurological Society and the New York Academy of Medicine, Section of Neurology and Psychiatry, and published in abstract form in the proceedings of those societies appearing in the November 1939 issue of the ARCHIVES, page 968.

1. Gray, H.: Anatomy of the Human Body, revised and re-edited by W. H. Lewis, ed. 27, London, Longmans, Green & Co., 1938, p. 993, fig. 898.

Review of the literature led to three interesting observations: First, it revealed afresh and in true perspective the epoch-making character of the investigations carried out on the brains of animals between 1870 and 1910 by that brilliant school of English physiologists led by Ferrier, Horsley and Sherrington, in which the motor area for the lower extremity was minutely mapped out on the lateral surface of the cerebrum in many animals, ranging from the cat to the gorilla. On the other hand, in contrast to the richness of the experimental data, there was found in the literature of the same period a striking paucity of reliable observations obtained directly from the human brain—especially observations regarding the position of the primary motor centers for the lower extremity.

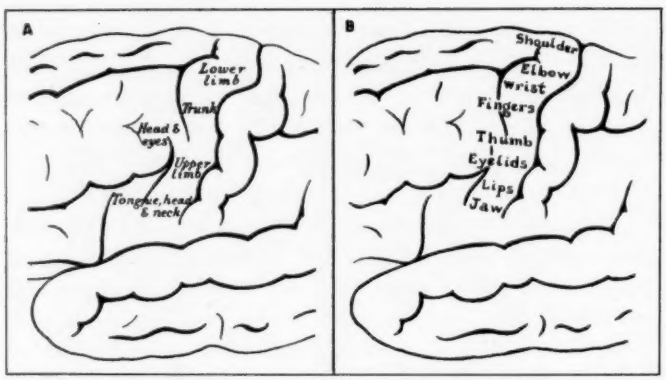


Fig. 1.—The primary motor centers of the human brain (*A*) according to Gray [1] and (*B*) according to my observations. Compare the positions of the shoulder area in the two sketches and note that in my diagram the primary leg centers are unrepresented on the lateral surface of the hemisphere.

Finally, it became evident in reading the literature that the anatomists and clinicians, in the absence of adequate observations on the human brain with regard to the leg centers, had tended to accept as true for the brain of man the cortical representation of these functions worked out by the physiologists on the brains of animals.

The first part of this paper consists of a historical and critical review of the literature on which is based the common and (in my opinion) erroneous concept that the primary motor centers for the lower extremity are situated on the lateral convexity of the cerebral hemisphere. The second part of the paper consists of a report of my personal observations, made on the exposed human brain at the operating table, which tend to show that in man the primary motor centers for the upper extremity commonly extend entirely up to the superior mesial border of the

cerebral hemisphere, and that the centers for the leg, as a rule, are not primarily represented on the lateral surface of the cerebrum.

REVIEW OF THE LITERATURE

EARLY EXPERIMENTAL WORK (1870-1914)

As late as 1870, that is, within the lifetime of men now living, the question whether there was any focal representation of motor function

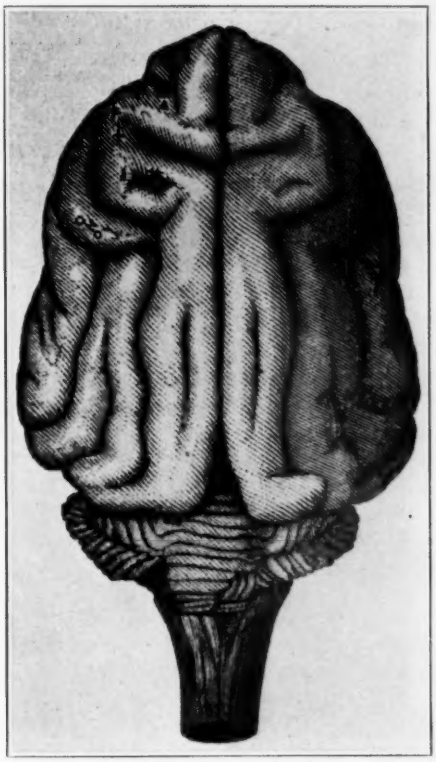


Fig. 2.—Fritsch and Hitzig initiated a new technic for studying the physiology of the brain, and demonstrated for the first time, in 1870, that focal motor responses could be elicited from the contralateral extremities by stimulating the cerebral cortex (of dogs) with electric currents. This figure, reproduced from their original article, shows "centers," for the neck muscles (+ +), for the forelimb (#), for the "hindlimb" (*O O*), and for the face (△).

within the brain was still being vigorously debated; the physiologists of the day were divided into widely divergent, and even hostile, schools of thought, with such great men as Flourens and Magendie strongly denying that cerebral localization of motor function existed.

In 1870, however, Fritsch and Hitzig [2] applied an electric current to isolated points on the exposed brain of a dog and observed focal responses in the contralateral extremities (fig. 2). This observation was destined to revolutionize the methods of investigation and knowledge of cerebral function. Three years later, in 1873, Ferrier,[3] who was then working obscurely in the West Riding Lunatic Asylum, published an epoch-making paper describing, in detail, constant focal response in the contralateral extremities obtained by stimulating fixed points of the brain in cats, dogs, rabbits and other animals. In 1874, he followed this with the first of similar studies,[4] outlining in great detail the motor cortex of monkeys (fig. 3). So carefully were his experiments performed that their correctness has since been repeatedly confirmed, and Ferrier's then revolutionary thesis remains today unchallenged.

In 1887, Horsley and his associates,[5] beginning where Ferrier had left off, instituted "a further minute research" into the motor areas of

---

2. Fritsch, G., and Hitzig, E.: Ueber die elektrische Erregbarkeit der Grosshirns, Arch. f. Anat., Physiol. u. wissensch. Med., 1870, pp. 300-332.

3. Ferrier, D.: Experimental Researches in Cerebral Physiology and Pathology, West Riding Lunatic Asylum M. Rep. **3**:30-96, 1873.

4. (*a*) Ferrier, D.: On the Localization of the Functions of the Brain, Proc. Roy. Soc., London **22**:229-232, 1874; (*b*) Experiments on the Brain of Monkeys: I, ibid. **23**:409-431, 1874-1875; (*c*) The Croonian Lecture: Experiments on the Brain of Monkeys (Second Series), Phil. Tr. Roy. Soc., London **165**:433-488, 1876; (*d*) The Localization of Cerebral Disease, Being the Goulstonian Lectures of the Royal College of Physicians for 1878, Brit. M. J. **1**:399, 443, 471, 515, 555 and 591, 1878; The Localization of Cerebral Disease, New York, G. P. Putnam's Sons, 1879; (*e*) The Function of the Brain, New York, G. P. Putnam's Sons, 1886; (*f*) The Croonian Lecture on Cerebral Localization, Brit. M. J. **1**:1289, 1349, 1413 and 1473, 1890; **2**:10 and 68, 1890; Lancet **1**:1225, 1287, 1343 and 1409, 1890; **2**:8 and 64, 1890; The Croonian Lectures on Cerebral Localization, Delivered Before the Royal College of Physicians, London, Smith, Elder & Co., 1890. (*g*) Ferrier, D., and Yeo, G. F.: A Record of Experiments on the Effects of Lesions of Different Regions of the Cerebral Hemispheres, Phil. Tr. Roy. Soc., London **175**:479-564, 1885.

5. (*a*) Beevor, C., and Horsley, V.: A Minute Analysis (Experimental) of the Various Movements Produced by Stimulating in the Monkey Different Regions of the Cortical Center for the Upper Limb, as Defined by Professor Ferrier, Phil. Tr. Roy. Soc., London, s.B **178**:153-168, 1887; (*b*) A Further Minute Analysis by Electric Stimulation of the So-Called Motor Region of the Cortex Cerebri in the Monkey (Macacus Sinicus), ibid. **179**:205-256, 1888; (*c*) An Experimental Investigation into the Arrangement of the Excitable Fibres of the Internal Capsule of the Bonnet Monkey (Macacus Sinicus), ibid. **181**:49-88, 1890; (*d*) A Record of the Results Obtained by Electric Excitation of the So-Called Motor Cortex and Internal Capsule in an Orang-Outan (Sinica Satyrus), ibid. **181**:129-158, 1890. (*e*) Horsley, V., and Schäfer, E. A.: A Record of Experiments upon the Functions of the Cerebral Cortex, ibid. **179**:1-47, 1888. (*f*) Semon, F., and Horsley, V.:

the cerebrum of the monkey. Working with the utmost scientific and physiologic precision (fig. 4 *A*), these men, in a series of brilliant studies, established within the brief span of four years the minute representation of motor function in the cerebral cortex, the internal capsule and the spinal cord of monkeys; they climaxed their researches with an elaborate investigation of the motor areas in the highly organized brain of the orang-utan (fig. 4 *B*).

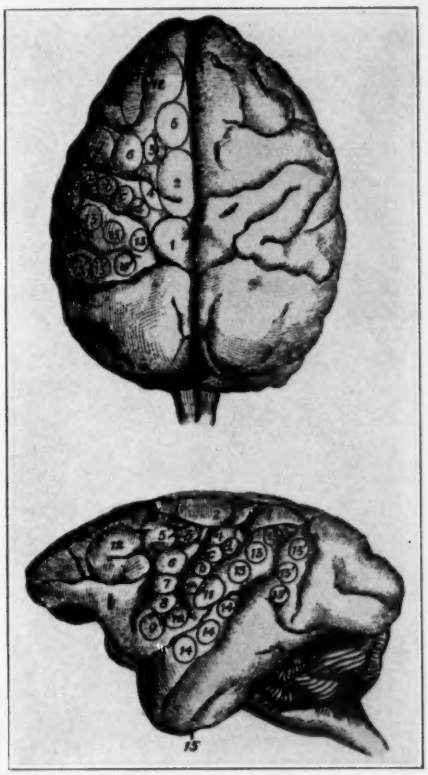


Fig. 3.—Ferrier, in 1873, confirmed the observations of Frisch and Hitzig and extended them to the brains of a great number of other animals, including the monkey (above). His experiments may be said to have established the fact that there is localization of function in the cerebrum.

An Experimental Investigation of the Central Motor Innervation of the Larynx, ibid. **181**:187-211, 1890. (*g*) Gotch, F., and Horsley, V.: Observations upon the Electromotive Charges on the Spinal Cord, Following Electric Excitation of the Cortex Cerebri: Preliminary Report, Proc. Roy. Soc., London **45**:18-26, 1888-1889; (*h*) The Croonian Lecture: On the Mammalian Nervous System, Its Function, and Their Localizations Determined by an Electrical Method, Phil. Tr. Roy. Soc., London, s.B **182**:267-526, 1891.

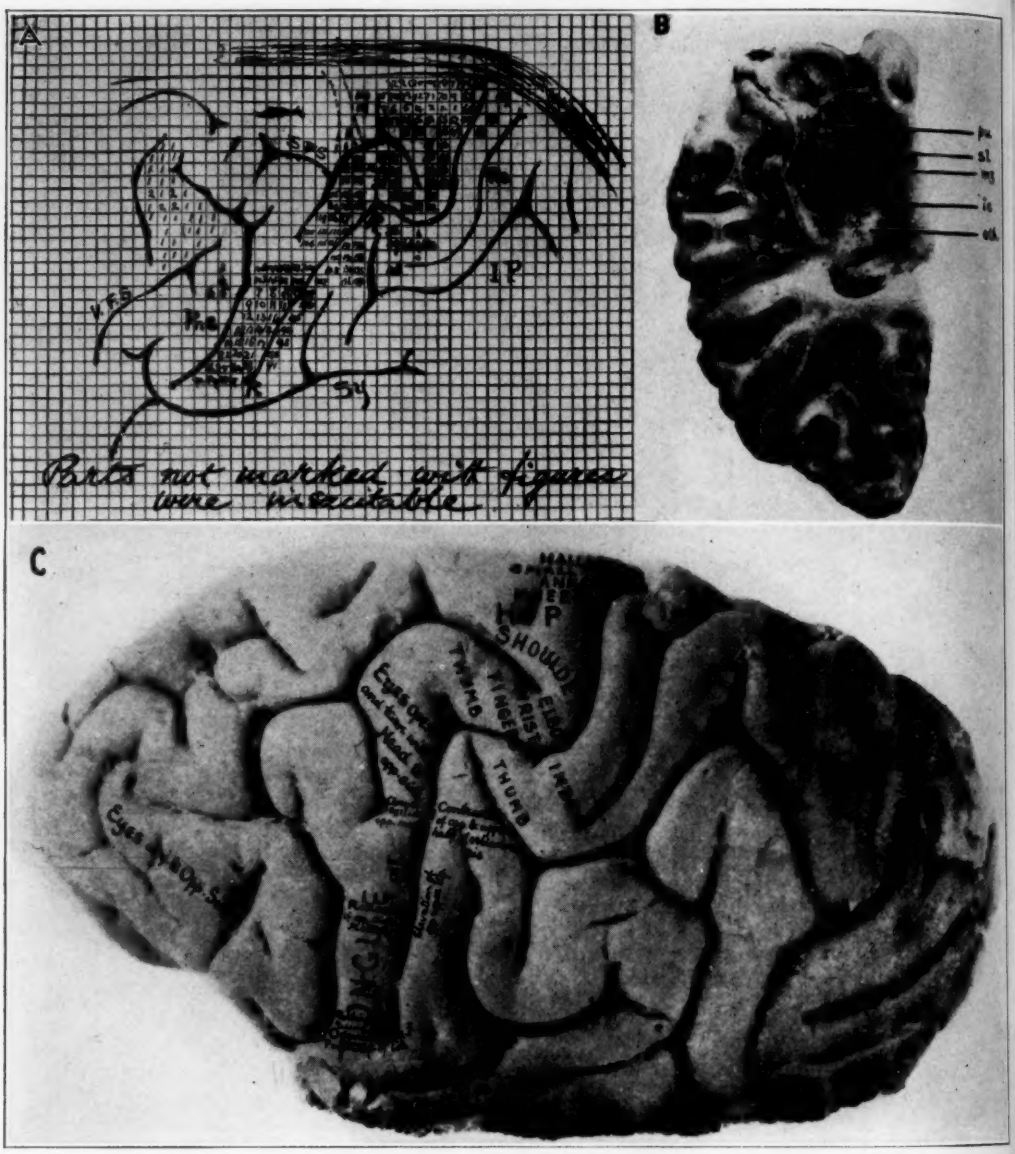


Fig. 4.—Beevor and Horsley (1887 to 1890) confirmed and extended the work of Ferrier. Introducing exquisite laboratory methods (*A* and *B*), these investigators reexamined in minute detail the motor cortex of the monkey, including the highly developed brain of the orang-utan (*C*).

In 1902 and 1903 the stamp of confirmation and finality was seemingly placed on the localization of motor function in the brain by Sir Charles Sherrington and his co-workers.[6] Taking up the work where Horsley had left off, they "mapped out," with painstaking care (fig. 5 *A*),

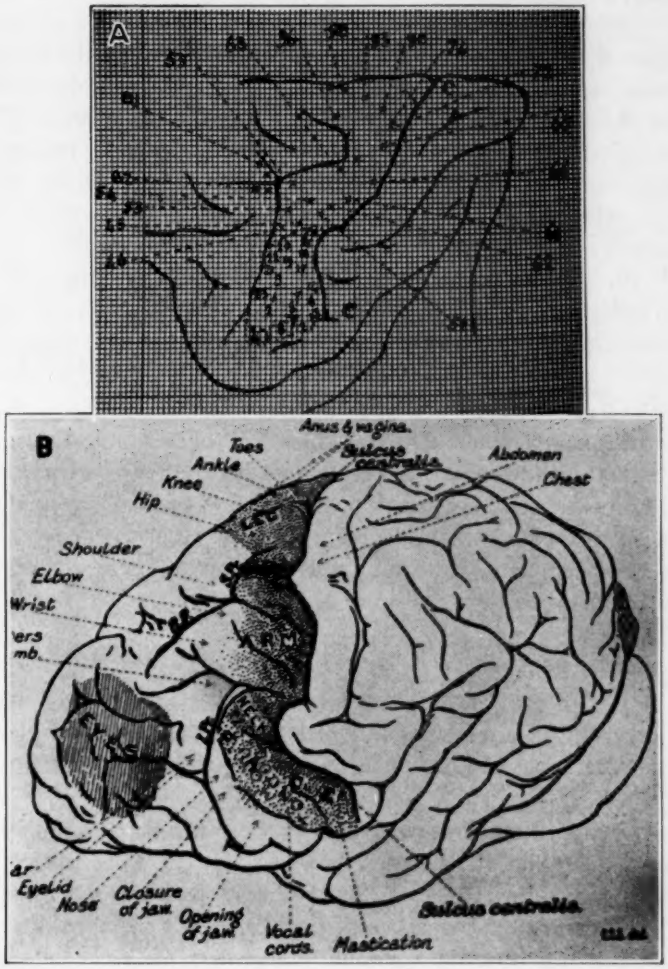


Fig. 5.—Sherrington and his school (1901 to 1906) continued Horsley's work, and investigated with the utmost precision (*A*) the motor cortex of the higher anthropoid apes. The lower chart (*B*) is a map of the motor areas of the chimpanzee's brain as determined by Sherrington and Grünbaum.

6. Sherrington, C. S., and Grünbaum, A. S. F.: Localization in the Motor Cerebral Cortex of the Anthropoid Ape, Tr. Path. Soc. London **53**:127-136, 1902. Grünbaum, A. S. F., and Sherrington, C. S.: Observation on the Physiology of the

(Footnote continued on next page)

the motor areas on the cortex of the great anthropoid apes, including the chimpanzee and the gorilla, the brains of which are so highly developed that even in Sherrington's own illustrations they resemble, in a striking manner, the brain of man (fig. 5 *B*).

These three great investigators, therefore, within the short space of thirty years, established the fact that focal representation exists within the brain of animals, thereby apparently ending one of the major controversies regarding the nature and function of the brain which had divided philosophic and scientific thought since ancient times. For this reason it is not difficult to understand the tremendous prestige in the scientific world which attached itself to these men and the dominant influence which their experimental work exerted whenever localization of motor function in the brain—even in the human brain—was being considered. Under these circumstances it was only natural, should clinical evidence to the contrary be lacking, for physicians and surgeons to assume that the localizations which these great leaders had found to hold true in so many species of mammals, including the higher anthropoid apes, would likewise hold true for man.

Conclusion.—The fact that these men had found in animals, including the great apes, the primary motor centers for the lower extremity to be situated on the lateral convexity of the cerebral hemisphere undoubtedly influenced to a considerable degree, as will be seen, the general concept which was formulated regarding the position of these centers in the human brain.

EARLY OBSERVATIONS ON THE HUMAN BRAIN (1874–1914)

A review of clinical literature for the forty years from 1874 to 1914 yields descriptions of 74 cases in which the human brain was electrically stimulated at the operating table and motor responses were recorded[7] (table 1).

Movements of the lower extremities were noted in 6 of these cases (table 2). In 5 of the 6 cases, however, factors were present which greatly reduced the value of the observations for any fundamental physiologic or anatomic purposes. In 3 cases, for instance, the records indicate that the electric currents used were of great and entirely unphysiologic strength, and although movements of the leg unquestionably were obtained, it seems certain that these were part of gross "mass" movements rather than truly focal responses. In 2 other cases the presence of expanding subcortical lesions, either proved at operation or strongly suggested by clinical evidence, demands that the value of these

---

Cerebral Cortex of the Anthropoid Apes, Thompson, Yates & Johnston Lab. Rep. **5**:55-58, 1903. Roaf, H. E., and Sherrington, C. S.: Experiments in Examination of the "Locked-Jaw" Induced by Tetanus Toxin, J. Physiol. **34**:313-331, 1906.

TABLE 1.—*Cases of Electrical Stimulation of the Human Cortex Reported Between 1874 and 1914* *

Case No.	Indentification: Patient	Age	Authors	Nationality	Comment
1	M. R.	30	Bartholow [7a]	American	Epithelioma of scalp—postcentral and parasagittal. Needle electrodes plunged through dura into cortex on right and left sides; pure sensory responses and movement of arms and legs obtained
2	F. R.	..	Sciamanna [7b]	Italian	Movement of alae nasi, fingers, forearm, head, tongue and eyelids (observations carried out, in part, on a fresh human cadaver)
3	"Infant 6 wk."		Horsley (Brain **7**: 228-243, 1884-1885)	British	Electrical stimulation applied to a meningocele, resulting in movements of eyes
4	O. S. H.	10	Horsley [7d]	British	Response elicited from facial area
5	W. B.	20	Keen [7l]	American	Hand, wrist and face area stimulated; wrist area excised
6	J. W. G.	35	Lloyd and Deaver [7r]	American	Response in face and fingers
7	.....	27	Nancrede [7s]	American	Movement of thumb
8	.....	..	Kammerer [7t]	American	No response
9	R. L.	39	Horsley [7g]	British	Response in wrist, finger, shoulder and arm, and thumb
10	M.	14	Mills [7p] and Hearn, p. 269	American	Response in wrist, eyes, mouth and head
11	C. J.	39	Keen [7m]	American	Movements of face, thumbs, fingers and head
12	G. H.	23	Keen [7m]	American	Stimulation, but no response
13	E. C. P.	56	Keen [7m]	American	Stimulation, but no response
14	S. W.	27	Mills and Keen [7o]	American	Responses in shoulder, arm and leg
15	.....	36	Hochenegg [7u]	Austrian	Movements of fingers
16	T. F.	19	Ranson [7v]	British	Movement of fingers and thumb on direct cortical stimulation; later peculiar sensory phenomenon obtained by plunging needle electrodes through scalp in decompression area
17	L. G.	6	Gerster and Sachs [7w]	American	Movements of right arm
18	W. C. H.	20	Gerster and Sachs [7w]	American	Movements of right arm and mouth
19	H. L.	24	Gerster and Sachs [7w]	American	Location of right arm area by electrical stimulation; excision
20	.....	9	Parker and Gotch [7y]	British	Movements of thumb and wrist
21	.....	..	Bidwell and Sherrington [7z]	British	Movements of leg
22	.....	36	Dana [7a']	American	Stimulation by plunging needle electrodes through scalp in decompression area; massive movements of arm and leg
23	.....	..	Diller and Buchanan [7b']	American	Movements of thumb
24	.....	25	Stieglitz and Gerster (assisted by Sachs) [7x]	American	Movements of fingers and hand; stimulation made through unopened dura
25	"Young man"		Warnots [7c']	Belgian	Focal movements of upper extremity on cortical stimulation; convulsion of lower extremity on stimulation close to pacchionian granulation
26	A. A.	29	Laycock [7d']	British	Stimulation of cortex with galvanic and faradic currents; no response
27	J. B. G.	24	Fischer and Bryant, cited by Starr p. 62 [7e']	American	Movements of hand
28	J. H.	22	Fischer and Woolsey, cited by Starr, p. 63 [7e']	American	Response in hand
29	A. D.	20	Fischer and Kelley, cited by Starr, p. 64 [7e']	American	Response in hand
30	K.	23	Vierordt [7f']	German	Cortical tuberculosis. Trephination at "center for upper and lower limbs;" stimulation with strong faradic current produced simultaneous contractions of all limbs

* The correct chronologic order in which the various authors first reported cases has been observed so far as possible in the preparation of this table.

TABLE 1.—*Cases of Electrical Stimulation of the Human Cortex Reported Between 1874 and 1914—Continued*

Case No.	Identification: Patient	Age	Authors	Nationality	Comment
31	S. G.	6	Angell [7g]	American	Extradural stimulation of cerebral convexity produced contraction of arm
32	W. M.	52	Keen [7a] (observation M, by Lamacq [7j] p. 518)	American	Movements of fingers, wrist, arm and shoulder
33	.....	30	Schlesinger [7h]	German	Weak current, no response; strong current, mass movements of arms and leg; no focal responses
34	.....	25	Guthrie [7i]	British	Response of face only
35	M. G.	8	Keen, cited by Lamacq,[7j] observation B, p. 508	American	Movement of forearm, elbow, wrist and finger
36	C. W.	15	Keen, cited by Lamacq,[7j] observation C, p. 509	American	Movement of arm, wrist, fingers and face
37	P. A.	57	Keen, cited by Lamacq,[7k] observation D, p. 510	American	Movement of shoulder, elbow and wrist
38	R.	29	Keen, cited by Lamacq,[7j] observation E, p. 510	American	Electrical stimulation with faradic current; no movements, but sensation in the back, similar to those preceding attacks
39	J. M.	7	Keen, cited by Lamacq,[7j] observation F, p. 510	American	Movements of fingers and elbow joint
40	R. M.	3	Keen, cited by Lamacq,[7j] observation G, p. 511	American	Faradic stimulation without any movements
41	M. J.	21	Keen, cited by Lamacq,[7j] observation H, p. 511	American	Faradic stimulation with resulting movements of fingers, thumb, wrist and face
42	S. F.	12	Keen, cited by Lamacq,[7j] observation I, p. 513 (1st operation)	American	Faradic current; movement of the two eyes, wrist and fingers
43	S. F.	12	Keen, cited by Lamacq,[7j] observation I, p. 513 (2d operation)	American	Movements of thumb and fingers
44	F. H.	26	Keen, cited by Lamacq,[7j] observation J, p. 515	American	Flexion of forearm and arm
45	J. A. W.	3	Keen, cited by Lamacq,[7j] observation K, p. 516	American	Movement of leg
46	K. H.	23	Keen, cited by Lamacq,[7j] observation L,	American	Faradic stimulation; no response
47	Case 1		Bechterew; cited by Lamacq,[7j] p. 491	Russian	Electrical stimulation; (1) conjugate deviation of head and eyes to opposite side, (2) flexion of elbow
48	Case 2		Bechterew; cited by Lamacq,[7j] p. 491	Russian	Electrical stimulation; (1) movements of opposite side of face, (2) clonic movements of the opposite thumb, (3) clonic movement of fingers of opposite side
49	Observation 1**		Mills and Frazier [7q]	American	Movements of eyelid and face (unipolar faradic stimulation)
50	Observation 2		Mills and Frazier [7q]	American	Movements in jaw
51	Observation 3		Mills and Frazier [7q]	American	Movements of jaw, face and shoulder
52	Observation 4		Mills and Frazier [7q]	American	Movements of shoulders, neck and pectoral muscle
53	Observation 5		Mills and Frazier [7q]	American	Flexion of arm at elbow, followed at once by generalized convulsions
54	Observation 6		Mills and Frazier [7q]	American	No response

** Case reported in detail by J. W. McConnell (Univ. Pennsylvania M. Bull. **18**: 156-159. 1905-1906).

TABLE 1.—*Cases of Electrical Stimulation of the Human Cortex Reported Between 1874 and 1914—Continued*

Case No.	Identification: Patient	Identification: Age	Authors	Nationality	Comment
55	Observation 7		Mills and Frazier [7q]	American	No response
56	Observation 8		Keen,† cited by Mills and Frazier [7q]	American	Movements of fingers and wrist
57	Observation 9		Keen,† cited by Mills and Frazier [7q]	American	Electrodes introduced between bone and dura for indefinite distance; contractions of hand and leg (small type)
58	Observation 10		Keen,† cited by Mills and Frazier [7q]	American	Responses of arm and leg
59	.....	32	Cushing and Thomas [7l']	American	Movements of toes, ankles, thigh and leg
60	.....	15	Cushing [7m']	American	Movements of tongue, jaw, lips, thumb, fingers; flexion of elbow; sensation in hand and fingers
61	.....	44	Cushing [7m']	American	Movements of vocal cords and of thumb; sensation in index fingers and back of hands
62	Observation I-1		Krause,[7n'] p. 299	German	Movements of fingers, wrist and elbow
63	Observation I-2		Krause,[7n'] p. 303	German	Movements of face, finger and wrist
64	Observation I-3		Krause,[7n'] p. 309	German	Movements of lips, finger and wrist
65	Observation I-4		Krause,[7n'] p. 312	German	Extension of arm; extension of forearm at elbow; movements of mastication
66	"Case 1"		Krause,[7n'] p. 314	German	Movements of lips, eyelids, fingers, thumb, wrist and elbow
67	"Case 8"		Krause,[7n'] p. 316	German	Facial movements
68	Observation I-10		Krause [7n']	German	Movements of face and tongue
69	Observation I-11		Krause [7n']	German	Movements of fingers
70	Observation I-13		Krause,[7n'] p. 352	German	Movements at shoulder, elbow and wrist
71	Observation I-14		Krause,[7n'] p. 388	German	Movements of shoulder, elbow and wrist
72	Observation I-15		Krause,[7n'] p. 394	German	Movements of face, fingers, forearm and hand
73	Observation I-17		Krause [7n']	German	Stimulations
74	Observation I-18		Krause [7n']	German	Indentification of left facial area; excision (plate XXXI, book II; plate VII, book I)

† Cases contributed by Keen in personal communications to the authors (not reported elsewhere).

TABLE 2.—*Cases from Table 1 in which Responses in the Lower Extremity were Reported*

Case	Serial Number in Table 1	Author	Critical Comment
1	21	Bidwell and Sherrington [7s].....	Unphysiologic current used
2	14	Mills and Keen [7o].....	Unphysiologic current used
3	25	Warnots [7c'].....	Unphysiologic current used
4	59	Cushing and Thomas [7l'].....	Subcortical cyst in rolandic area
5	45	Keen, cited by Lamacq [7j'].....	Unphysiologic current used; subcortical tumor suspected
6	58	Keen, cited by Mills and Frazier [7q]	Arm area extended to superior mesial border of hemisphere

cases for topographic studies of the normal brain be seriously challenged. In the last of this group of 6 cases evidence suggested that the cortical representation of the lower extremity was not on the lateral, but on the mesial, surface of the cerebrum.

Because of their particular interest in the present study, these cases are reviewed in considerable detail in the pages which follow.

CASE 1 (table 2).—*Focal convulsion of right leg. Craniotomy. Cortical stimulation with electric currents of great strength. Movements of leg obtained. Excision of supposed leg center, but no resultant weakness in leg thereafter. Case reported by Bidwell and Sherrington.*[7z]

7. (*a*) Bartholow, R.: Experimental Investigation into the Functions of the Human Brain, Am. J. M. Sc. **67**:305-313, 1874. (*b*) Sciamanna, E.: Gli avversari della localizzazion cerebrali, Arch. di psichiat. **3**:208-215, 1882. (*c*) Horsley, V.: Brain Surgery, Brit. M. J. **2**:670-675, 1886; (*d*) Remarks on Ten Consecutive Cases of Operations upon the Brain and Cranial Cavity to Illustrate the Details and Safety of the Methods Employed (with a Table), ibid. **1**:863-865, 1887; (*e*) A Note on the Means of Topographical Diagnosis of Focal Disease Affecting the So-Called Motor Region of the Cerebral Cortex, Am. J. M. Sc. **93**:342-369, 1887; (*f*) Case of boy, O. S. H., aged 10 years, reported by Beevor and Horsley,[5d] page 152 (same as case 5,[7d] and also a case reported by Lamacq [7j']); (*g*) Case of man, R. L., aged 39, reported by Beevor and Horsley,[5d] page 154 (same as case V [7h] and case V. K. L., reported by Lamacq [7j']); (*h*) Remarks on the Surgery of the Central Nervous System, Brit. M. J. **2**:1286-1292, 1890; (*i*) The Linacre Lecture on the Function of the So-Called Motor Cortex of the Brain, ibid. **2**:121-132, 1909; (*j*) Abstract of the Brown Lectures on Experimental Sectioning of the Corpus Callosum, Lancet **2**:1211-1213, 1886; (*k*) On Tactile Sensibility, Practitioner **20**:581-596, 1904. (*l*) Keen, W. W.: Three Successful Cases of Cerebral Surgery, Including: (1) The Removal of a Large Intracranial Fibroma; (2) Excision of Damaged Brain Tissue; and (3) Exsection of the Cerebral Center for the Left Hand, with Remarks on the General Technique of Such Operations, Am. J. M. Sc. **96**:328-356 and 452-465, 1888; (*m*) Five Cases of Cerebral Surgery: I and II for Epilepsy Following Trauma; III for Insanity Following Trauma; IV for Cerebral Tumor; and V for Defective Development, ibid. **102**:219-238, 1891; (*n*) Five Cases of Brain Tumor in Three of Which Operation Was Done: Two Operative Recoveries; Ultimate Death in All, ibid. **107**:38-52 and 107-123, 1894. (*o*) Mills, C., and Keen, W. W.: Jacksonian Epilepsy: Trephining; Removal of Small Tumor, and Excision of Cortex, Am. J. M. Sc. **102**:587-600, 1891. (*p*) Mills, C. K.: Cerebral Localization in Its Practical Relations, Brain **12**:233-288 and 358-406, 1890. (*q*) Mills, C. K., and Frazier, C. H: The Motor Area of the Human Cerebrum, Its Position and Subdivisions, with Some Discussions of the Surgery of This Area, Univ. Pennsylvania M. Bull. **18**:135-147, 1905-1906. (*r*) Lloyd, J. H., and Deaver, J. B.: A Case of Focal Epilepsy Successfully Treated by Trephining and Excision of Motor Centers, Am. J. M. Sc. **96**:477-487, 1888. (*s*) Nancrede, C. B.: Two Successful Cases of Brain Surgery, M. News, Philadelphia **53**:585-588, 1888. (*t*) Kammerer, F.: A Case of Sarcoma of the Dura Mater, M. Rec. **36**:569, 1889. (*u*) Hochenegg, J.: Two Cases of Epilepsy Treated Surgically, Wien. klin. Wchnschr. **5**:174-176, 1892. (*v*) Ranson, W. B.: A Case Illustrating Kinaesthesis, Brain **15**:437-442, 1892. (*w*) Gerster, A. G., and Sachs, B.: The Surgical Treatment of Epilepsy,

A youth aged 15 had been suffering for five years with jacksonian seizures, starting in the right leg.

On April 23, 1895, "a large square flap [of skin] about 3 inches wide, having its anterior edge just behind the coronal suture, . . . was reflected downwards. A trephine with an inch crown was applied just behind the line of the fissure of Rolando; and again, more anteriorly, the intervening bone removed with bone forceps. The dura mater . . . was opened . . . and reflected. The fissure of Rolando was exposed with a large vein lying in it. The cerebral substance at the lower part of the exposed area looked discoloured, so the opening was enlarged downwards by removing a further disc of bone with the trephine. The whole of the discoloured area thus exposed was about the size of a four penny piece and was freely excised with a knife to a depth of three-quarters of an inch. There was some bleeding from the . . . substance, which was controlled by a stream of 1 in 20 carbolic acid solution.

Am. J. M. Sc. **104**:503-508, 1892. (*x*) Stieglitz, L., and Gerster, A. G.: Report of a Case of Cystic Tumor on the Brain Operated upon with Success, ibid. **105**:620-627, 1893; New York M. J. **57**:114-115, 1893. (*y*) Parker, R., and Gotch, F.: A Case of Focal Epilepsy: Trephining, Electric Stimulation and Excision of Focus; Primary Healing; Improvement, Brit. M. J. **1**:1101-1103, 1893. (*z*) Bidwell, L. A., and Sherrington, S. C.: Focal Epilepsy: Trephining and Removal of Small Haemorrhagic Focus; No Improvement; Removal of Part of Leg Centre After Electrical Stimulation, ibid. **2**:988-998, 1893. (*a'*) Dana, C. L.: An Experimental Study of the Seat of Cutaneous Sensations, M. Rec. **43**:578-579, 1893. (*b'*) Diller, T., and Buchanan, J. J.: A Case of Sub-Cortical Cyst of the Lower Part of the Left Ascending Parietal Convolution: Operation; Recovery, Am. J. M. Sc. **106**: 14-23, 1893. (*c'*) Warnots, L.: Report of case: Sur la chirurgie cérébrale, Assoc. franç. de chir., Proc.-verb. **1**:480-486, 1893. (*d'*) Laycock, G. L.: A Case of Intracranial Injury, with Extensive Destruction of Brain Substance About the Rolandic Area, and Loss of the So-Called Muscular Sense (with Phototype), Australian M. J. **15**:313-320, 1893. (*e'*) Starr, M. A.: Brain Surgery, New York, William Wood & Company, 1893. (*f'*) Vierordt, O.: Ueber die operative Behandlung sub-cortical gelegener Hirntumoren, Fortschr. d. Med. **12**:493-510, 1894. (*g'*) Angell, E. B.: A Case of Infantile Hemiplegia, Imbecility, and Epilepsy: Craniotomy; Marked Improvement, J. Nerv. & Ment. Dis. **19**:656-663, 1894. (*h'*) Schlesinger, H.: Report of Case, Neurol. Centralbl. **14**:702, 1895. (*i'*) Guthrie, L. B.: A Case of Violent Jactitation, of Twenty-Two Years' Duration, Affecting Chiefly the Left Arm and Leg, Treated by Trephining and Excision of the Arm-Center in the Right Motor Cortex: Result and Remarks, Proc. Roy. M. & Chir. Soc. London **9**:63-81, 1896-1897. (*j'*) Lamacq, L.: Les centres moteurs corticaux du cerveau humain déterminés d'après, les effets de l'excitation faradique des hémisphères cérébraux de l'homme, Arch. clin. de Bordeaux **6**:491-524 and 568-590, 1897. (*k'*) Cushing, H.: Presentation of Three Cases: (1) Decompressive Craniotomy for Brain Tumor; (2) Gasserian Ganglion Operation for Major Neuralgia; and (3) Exploratory Craniotomy for Jacksonian Epilepsy Originating in the Motor Area of the Lower Extremity, Bull. Johns Hopkins Hosp. **18**:144-145, 1907. (*l'*) Cushing, H., and Thomas, H. M.: Removal of a Sub-Cortical Cystic Tumor at a Second Stage Operation Without Anaesthesia, J. A. M. A. **50**:847-856 (March 14) 1908. (*m'*) Cushing, H.: A Note upon the Faradic Stimulation of the Post-central Gyrus in Conscious Patients, Brain **32**:44-53, 1909. (*n'*) Krause, F.: Chirurgie des Gehirns und Rückenmarks, Berlin, Urban & Schwarzenberg, 1908-1911; Surgery of Brain and Spinal Cord, New York, Rebman Company, 1909-1912.

"The wound healed completely within a week, and there was no loss of power in the foot or leg."

A second operation was performed on May 14, 1897, at which time the original opening "was enlarged by removing two further discs of bone, one above and the other posterior to the old opening, the intermediate bone being removed with bone forceps. The dura mater . . . was reflected downward. Dr. Sherrington, who had kindly lent the electrical apparatus, was good enough to superintend the stimulation of the cortex. . . . On applying a strong current just above the part [of the cortex] previously removed, movements of the foot and knee similar to the epileptic spasms were produced. . . . The area by stimulation of which these movements were produced was about the size of a sixpence, and was situated just above the discoloured area, previously removed. It was freely excised to a depth of ¾ inch with a knife, and bleeding stopped by a 1 in 20 carbolic lotion."

In the postoperative note which followed it was reported that "the wound was healed at the end of a week. There was absolutely no loss of power in the right leg and foot, and no impairment of any movement; there was no loss of sensation or fall in temperature of the limb; the knee jerks were natural, and there was no ankle clonus."

Comment.—Professor Sherrington remarked: "[At first] the currents were of moderate intensity. . . . No effects being obtained, the secondary coil was brought nearer the primary. . . . Each application of the current lasted about five seconds. . . . I hesitated to resort to more violent stimulation, [but] the intensity of the current was now increased and by successive shifts the secondary coil pushed up to 4 centimeters from the primary." A little further on, Sherrington referred to this current as, "physiologically speaking, very intense . . . a current quite unbearable." He was careful to add that "the degree to which the patient was under the influence of the anaesthetic . . . was quite trifling."

It is obvious from Sherrington's remarks that the current was excessive. However, using this current, the operator found a point stimulation of which set off movements of the foot and knee which were "similar to the epileptic spasms." Even with this excessively strong current, however, no responses of any sort were obtained from adjacent parts of the exposed cortex. It seems improper, therefore, to consider the "epileptic spasm" resulting as being a true focal response from the primary motor cortex.

More important, however, is the fact that excision of the area which the operator decided to be the center for movements of the lower extremity failed to produce even transient weakness of the leg or changes in reflexes, however slight. It is evident from this that the region taken to be the "leg area" could not have been the primary center for movements for this extremity, and that the movements obtained must have resulted from radiation of the excessive electric currents to the true motor cortex.

The evidence indicates, therefore, that in this case false localization of the leg center resulted from the use of currents of excessive strength.

CASE 2 (table 2).—*Sensory and motor jacksonian seizures of left arm and shoulder. Craniotomy. Stimulation of cortex with powerful currents yielding mass movements of entire right side of body. Excision of presumed leg center, without resulting paralysis. Case reported by Mills and Keen.*[70]

A woman aged 27 had suffered from sensory and motor seizures of the jacksonian type, involving primarily the left arm and shoulder. Cerebral exploration was undertaken to determine and, if possible, to eradicate the cause of these convulsions.

A description of the operation by Dr. Keen follows: "A large horseshoe flap [of skin] was made, and on turning this back no abnormal appearance of the skull was found. The centre pin of a 1½ inch trephine was now inserted 1.75 inch from the median line as before determined, the upper edge of the trephine reaching to a point 1 inch from the median line.

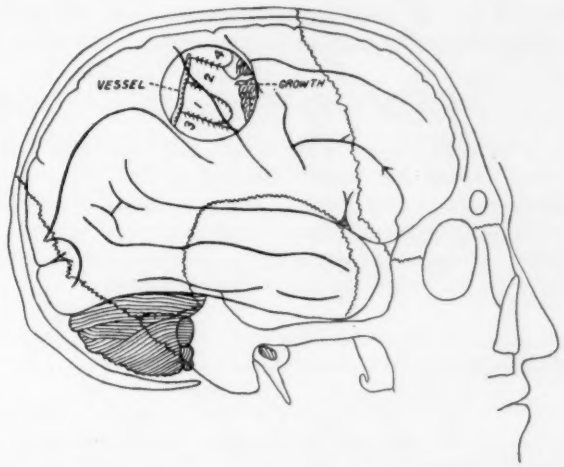


Fig. 6.—Operator's sketch from the case of Mills and Keen (case 2, table 2). Movement of the leg was described in this case, but was part of a massive reaction to currents of excessive and unphysiologic strength.

"[The dura was opened] . . . A fissure corresponding to the line of the fissure of Rolando was seen, and five convolutions were exposed [fig. 6].

"Careful investigations were then made with the faradic current with a view of determining the cortical centres exposed.

"Several spots were selected, marked 1, 2, 3 and 4 [see fig. 6]. The first electric tests were made at the spots 1 and 2. From the measurements that had been made, the fissure of Rolando was in the direction indicated by the line seen in the illustration.

"Electricity was first applied to the spot marked 1 for a moment only. Movement at once resulted, beginning in the upper extremity on the left side, the first movement being protraction and moderate adduction of the shoulder and upper arm. This was followed by a series of jerks, involving the upper, and to a more moderate degree, the lower arm. No differentiated movements of the hand and

arm, and no face or upper leg contractions, were observed. The left toes and foot, however, slightly flexed coincidently with the shoulder movement.

"A second application was made at the point marked 2. The effect of this excitation was again to produce decided shoulder and arm movements, with greater adduction and some protraction of the entire arm. The thigh was flexed upon the pelvis at an angle of about 130°, and the leg upon the thigh to about the same, with abduction of the thigh and extension of the toes and foot. At the same time, active, coarse, clonic movements diffused through both extremities. This series of movements of the left upper and lower extremities strongly resembled the spasms which occurred in the patient's ordinary attacks, with the exception that the head was not turned to the right, and no face movements were noted. The application was repeated at 2, with similar results, with the addition that the face and head turned to the left, and the head was drawn downward and to the left, chiefly by platysmic action. . . .

"With a pair of scissors and sharp bistoury, a portion of the cortex, three-quarters of an inch in diameter, was removed. It included all the cortical gray matter under the tumor and corresponding to the centre for the shoulder as ascertained by the battery. The arm, leg and face were carefully observed during excision, but this mechanical excitation was absolutely without effect in producing movements.

"After excision the electrodes were now applied to the points 3 and 4 on the border of the excision.

'Excitation at the point marked 3 flexed the elbow, hand and wrist with slight shoulder abduction, protraction closely following.

"Excitation at 4 caused primary movements of abduction and flexion of the thigh upon the pelvis, and the leg upon the thigh at an angle of 135 ° or 140 °. No foot movements or movements of the upper extremities occurred. In all the trials after the excision of the cortex the movements were confined to the left half of the body."

A note on the tenth postoperative day read: "She now has good use of both the left arm and the left leg, all movements being preserved."

Comment.—On first reading this report, it would appear that point *4* (fig. 6) represented the primary center for movements of the leg. On closer reading, however, this seems unlikely, for the following reasons: It is specifically stated in the operator's note that five convolutions were exposed in the trephine opening. On referring to the operative sketch, it will be observed that one convolution, the most posterior, runs in a vertical line directly parallel with the fissure of Rolando, and is presumably the precentral gyrus, while the other four convolutions, all anterior to the vertical one just mentioned, lie in a horizontal plane, and thus seem to be posterior portions of the frontal convolutions. It appears, therefore, on purely anatomic grounds, that the stimulation had been directed to the frontal or premotor regions (areas 6 ab or 8), and that actually the primary motor centers in the precentral gyrus had not been stimulated.

It is obvious that an unphysiologic current of great intensity was used, since stimulation at point *2* produced simultaneous movements of the face, neck, shoulder, arm, thigh, leg, foot and toes. The movement

elicited from point *4* was a "mass" movement of the entire extremity, rather than a focal response. Even then, the only active movement of the lower extremity of which one can be sure in reading the report is the "abduction flexion of the thigh upon the pelvis," because, with the patient lying on his back, "flexion of the leg upon the thigh" would be an inevitable, passive accompaniment of the former movement. Indeed, had not areas *1* and *2* already been excised, it seems likely that this mass response might have included the upper extremity as well as the lower. In any event, the results of cortical stimulation carried out with currents of such strength as to produce movements through an entire side of the body with a single application of the electrode can have no real value in determining the site of primary motor centers in the normal brain.

The area which the surgeon decided to be the primary center for movements of the shoulder was widely excised at the operating table. Yet, ten days after the operation, that is, as soon as sufficient time had elapsed for postoperative edema to subside, the patient had "good use of . . . the left arm . . . all movements being preserved." From this the conclusion is justified that the primary motor center for the shoulder was not excised, and hence was not correctly identified at the operating table. If this is so, it raises grave doubt that the cortical area immediately adjacent to the presumed shoulder area, which in turn was "identified" as the leg center, actually was the true primary center for the leg. An error so gross in one observation casts doubts on the accuracy of all the other observations.

On anatomic, physiologic and clinical grounds, therefore, it appears that this case is ill suited for purposes of topographic study.

CASE 3 (table 2).—*Generalized convulsions. Exploration of right central region. Single stimulation of supposed leg center produced convulsion starting in left leg and quickly involving entire left side of body. Case reported by Warnots.*[76]

A young man suffered from generalized convulsions. Exploration was carried out over the right cerebral hemisphere. "With a minimal current, I explored the principal centers for movements of the upper extremity, which responded physiologically. I then passed on to exploration of the centers for movements of the lower extremity; as soon as I had applied electrodes, a violent convulsion of the lower extremity took place, followed immediately by tonic and clonic movements of the entire corresponding half of the body. I proceeded with careful examination of the centers for the lower extremity, and ascertained that beneath the pacchionian granulations there was an area of yellow exudate about the size of a centime. This was removed, in spite of the rupture of a large vein which emptied into the superior longitudinal sinus."

Comment.—The only motor response described as a result of stimulation of the supposed leg area was a violent convulsion, which involved the entire contralateral side of the body—the arm as well as the leg.

The operator stated that after the convulsion he proceeded with a careful "examination" of the centers of the lower extremity and found—an area of yellow exudate! One is left in doubt, therefore, whether examination was electrical or visual.

Description and identification of the areas stimulated are completely lacking in the report, so that the case is practically worthless for any serious topographic studies. All that can be said is that if focal responses were elicited in the lower extremity, they were obtained from a region close to the superior mesial border of the hemisphere.

CASE 4 (table 2).—*Focal motor and sensory seizures in left leg for ten years. More recently, left hemiparesis, headache, vomiting and papilledema. Cerebral exploration. Focal responses in left leg following stimulation near superior mesial border of hemisphere. Disclosure and removal of large subcortical cyst from underlying brain. Case reported by Cushing and Thomas*[71] *and Cushing.*[7m]

A school teacher aged 32 had been suffering for ten years from "nervous attacks," associated with twitching of the muscles of the left calf. Consciousness was almost always retained, but during the ten years he had become unconscious six times. Two years before admission, for three months, he suffered from intense headache, associated temporarily with nausea, vomiting, diplopia, failing vision and weakness of the left arm and left leg. At the time of his admission to the hospital, in November 1905, he complained chiefly of loss of vision, weakness of the left leg and convulsive attacks.

Examination revealed secondary atrophy of both optic disks, a distinctly hemiplegic limp on the left, atrophy of the left leg, markedly exaggerated tendon reflexes in the left leg and a positive Babinski sign. All modalities of sensitivity were tested in the feet and legs, without discovering any abnormalities.

It was the preoperative impression "that the patient was suffering from an organic lesion situated in the upper part of the Rolandic region, involving the cortex itself or lying just below it. The fact that the seizures were so largely sensory in character pointed to the post-central convolutions, but as definite . . . paresis of the left leg occurred, [it was concluded] that the leg areas were also involved in the process."

Operations were performed in five stages, details of which may be found in the original articles. The essential features of the case, however, may be summarized as follows: When the dura was opened the brain protruded slightly. Identification of motor points was carried out with a faradic current. Cushing stated that, in addition to obtaining movements in the upper extremity, "in this patient, *for the first time,* I succeeded in eliciting clear-cut movements from the thigh, lower leg, and foot [fig. 7]." The precentral gyrus was of normal pinkish color. The gyri posterior to the central fissure, on the other hand, were distinctly yellow. The gyrus centralis posterior was evidently flattened, and of considerably more than its natural width; it was determined to explore through the crest of this convolution.

A longitudinal incision was accordingly made in this gyrus, and at a depth of about 1 cm. below the surface of the convolution the top of a thin-walled cyst came into view. By slow dissection and by enlargement of the incision until finally it measured about 5 cm. in length, the cyst was almost completely enucleated. At this stage a sketch of the partially dislocated cyst was made by Brödel (fig. 7). Removal of this cyst, however, disclosed the upper surface of a still larger cyst situated just beneath it. This, in turn, was shelled out of its bed. The patient withstood the procedure well and made an excellent recovery.

Comment.—In this case, a huge cyst, approximately 3 inches (7.6 cm.) in diameter, was observed lying just beneath a discolored and thinned postcentral gyrus—and to a large extent also beneath the pre-

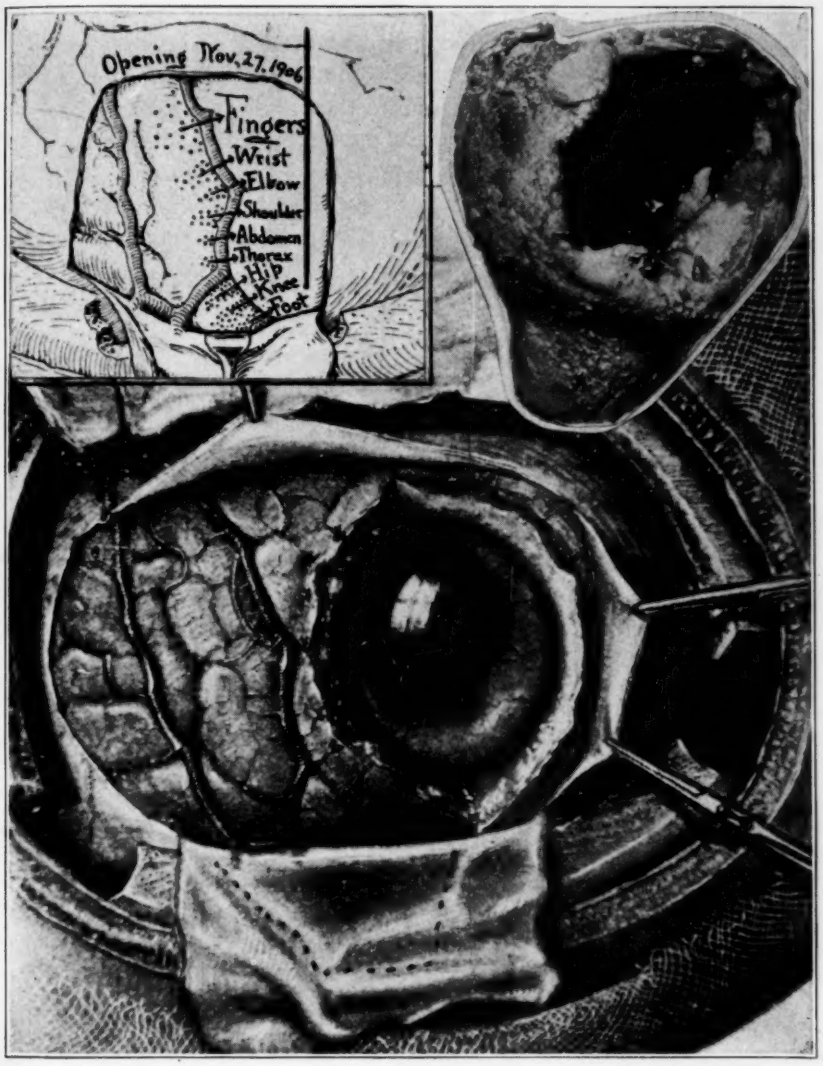


Fig. 7.—Cushing and Thomas reported in 1 case (case 4, table 2) movements of the leg following stimulation of the lateral surface of the cerebrum (upper left portion). However, the value of this case in determining normal cerebral topography may be questioned in view of the inevitable distortion of the cortex produced by the large subcortical cyst which was seen at operation. The photograph of the cyst after removal (upper right corner) is reproduced on the same scale as the main drawing (lower portion), made by Brödel when the cyst was only partially exposed and before rupture; ¾ actual size.

central gyrus—close to the superior mesial border of the hemisphere. The history of convulsions for ten years suggests that the cyst had been present and growing for that length of time. During this period an upward and outward "rolling" of the superior mesial border of the hemisphere overlying the cyst, with distortion of the normal topographic relationship in this part of the cortex, could hardly have been avoided.

It seems questionable, therefore, whether one is justified in accepting the observations in this case relative to the motor center for the leg as representing the true situation in the normal brain, especially when Cushing himself stated, in reporting this case, that in all his experience this was the only instance in which he had obtained focal movements of the lower extremity by stimulating the cerebral cortex.

CASE 5 (table 2).—*Focal seizures in the right arm of a child; subsequent paresis of arm. Left cerebral exploration; cortical excitation. Movements of right side of face and right arm and leg elicited. Excision of supposed "hand and elbow centers," apparently without resultant paralysis. Possibility of subcortical tumor not verified. Operation by Keen; case reported by Lamacq as observation K.*[71]

A child aged 3 was "suffering from epileptiform attacks consisting of a hysterical cry, associated with slow shaking of the right forearm. In the beginning these attacks were slight, so that the parents did not attribute any importance to them. Gradually, they became more frequent and more severe, and were limited to the right arm.

"During the last ten days before operation, the child abandoned, little by little, the use of the right arm, although he was naturally right handed. He was still able to use his right hand, but not so well as his shoulder.

"On July 8, 1897, a left parietal flap about 3 inches (7.5 cm.) square, paralleling the fissure of Rolando, was turned down by Dr. Keen. Before the dura mater was opened, the centers for the leg, arm and face were located. Superiorly, the center for the leg was delimited exactly to one partly exposed convolution. There were flexions of the toes and ankle and, after many stimulations, clonic movements of the entire limb, beginning in the thigh. These clonic movements were repeated fifteen or twenty times before ceasing. The center for the leg was 2.5 cm. to the left of the midline, in front of the fissure of Rolando, and, vertically, directly above the external auditory meatus, as nearly as one could see.

"Stimulation of point 2 on the precentral gyrus, near its anterior border, produced movements of the hand, especially flexion of the fingers and of the thumb.

"Stimulation of point 3 on the precentral gyrus, which was a little closer to the midline and just in front of the fissure of Rolando, produced flexion of the wrist, and on two occasions a typical attack, like that described in the beginning.

"Stimulation of point 4 at a spot 5 cm. further down on the precentral (7.7 cm. from the midline) gyrus, produced movements of the right side of the face and fluttering of the eyelids. The intermediate portions of the precentral gyrus were inexcitable, as was all of the postcentral cortex. The center for the shoulder was especially sought, but was never found. The current used easily made the operator's own index finger contract."

The center for the hand and elbow was then excised, an area of the cortex 1.6 cm. square being removed. However, after this, excitation of the remaining gray matter provoked movement of the hand and elbow, but no attack.

Comment.—This is one of the cases which Keen never reported directly, but descriptions of which he sent to Lamacq in a personal communication to be used at the latter's pleasure in a paper he was then preparing. The operator's sketch (fig. 8) is obviously incomplete.

Movements of the lower extremity undoubtedly followed electrical excitation of the cortex in this case. However, one may well question whether these responses were obtained from stimulation of primary motor centers in view of the fact that after excision of the areas "identified" as hand and elbow centers, stimulation of the remaining cortex still provoked motor responses in the hand and elbow.

The rapid course of the illness and the progressive paresis remain unexplained, and raise the question whether there was not present some obscure subcortical inflammatory or neoplastic disease, capable of producing distortion of the anatomic and physiologic relations of this part

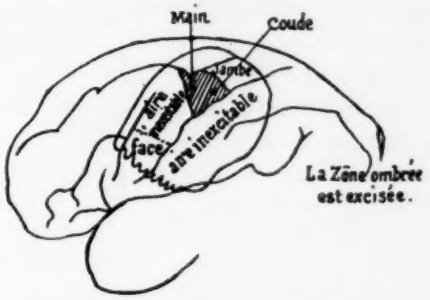


Fig. 8.—Diagram in the case of Keen, cited by Lamacq (case 5, table 2). Movements of the hand (*main*), elbow (*coude*) and leg (*jambe*) were obtained by electrical stimulation of the areas indicated on the chart. After excision of the presumed hand and elbow "centers," however, excitation of the remaining cortex still elicited all of the original movements, thus indicating that none of the areas stimulated were primary motor centers.

of the brain. Letters of inquiry were sent to the various hospitals and to some of the physicians with whom Dr. Keen had been associated in an effort to obtain more information about this case, but none could be had.

At best, therefore, the report of this case remains incomplete and unsatisfactory, and must be regarded as of dubious value for serious topographic studies.

Case 6 (table 2).—*Jacksonian seizures of left leg. Right craniotomy with cortical stimulation. Arm and shoulder area found to extend upward to midline. Responses elicited in leg only by stimulation of cerebrum at superior mesial border. Operation by Keen; case reported by Mills and Frazier (case 10).*[79]

A man aged 21 complained of jacksonian epilepsy, involving chiefly the left leg.

A large cranial flap was turned up, the mesial border of the exposure coming to within 2/5 inch (1 cm.), by actual measurement, of the midline.

The following is in Keen's own words:

"The bipolar faradic electrode was applied to the brain at the upper margin of the wound, in what was believed to be precentral and postcentral convolutions. The left arm was immediately thrown into spasm. . . . The opening apparently not being high enough to expose the leg centre, the bone was gnawed away to the sagittal suture and the flap of the dura was extended almost up to the margin of the superior longitudinal sinus. . . . No response was given from the postcentral gyrus, but immediately when the precentral was touched with the electrode the left leg was thrown into a general spasm, lasting about twenty seconds. This case is of much importance as indicating that the area for the lower extremity is close to the mesial surface."

Comment.—Stimulation of the cortex 2/5 inch (1 cm.) from the midline produced movements of the arm only, and actually it was not until a point on the mesial border of the hemisphere was exposed and stimulated that movements in the lower extremity were elicited. A graphic analysis of this case is given in figure 10.

Conclusion.—It is evident, therefore, that the clinical literature from 1874 to 1914 contains no data of true scientific worth to indicate that in man the primary motor area for the leg is situated on the lateral convexity of the cerebral hemisphere.

EARLY ATTEMPTS TO "MAP" THE HUMAN CORTEX; APPROPRIATION OF ANIMAL DATA (1874–1914)

The anatomists, neurologists and neurosurgeons early became infected with a desire to "map out" the brain of man as the physiologists had already "mapped out" the brains of animals. This they undertook to do in spite of the fact that at this time too few observations had been made directly on the human brain, especially pertaining to the lower extremity, to justify such an attempt. The result was that they were tempted to fill out the deficiencies and to supplement their own data on the human brain with observations made by the great physiologists on the brain of animals, particularly the higher anthropoid apes.

In the early days of neurosurgery, there were three pioneer schools: (1) the American school, with its center at Philadelphia, led by W. W. Keen; (2) the German school, ably represented by Fedor Krause, of Berlin, and (3) the English group of surgeons, dominated by Victor Horsley. Each of these schools furnished curious examples of this phenomenon of "trans-substitution."

In 1905, Mills and Frazier,[7q] representative of the American group, reported 10 cases of electrical stimulation of the human brain, in 7 of

which Frazier and in 3 Keen had performed operation (table 1, cases 49 to 58, inclusive). In 2 of these 10 cases no response whatever was obtained after cortical stimulation; in a third case bilateral generalized convulsions only were elicited. Of the remaining 7 cases, there was only 1, that of Keen, previously mentioned, in which electrical stimulation of the brain elicited movements of the lower extremity (table 1, case 58; table 2, case 6). This response of the leg was obtained only by stimulation of the brain exactly at the midline. Moreover, only one excitation of this area was made, and the single response which followed caused simultaneous movements of the entire leg.

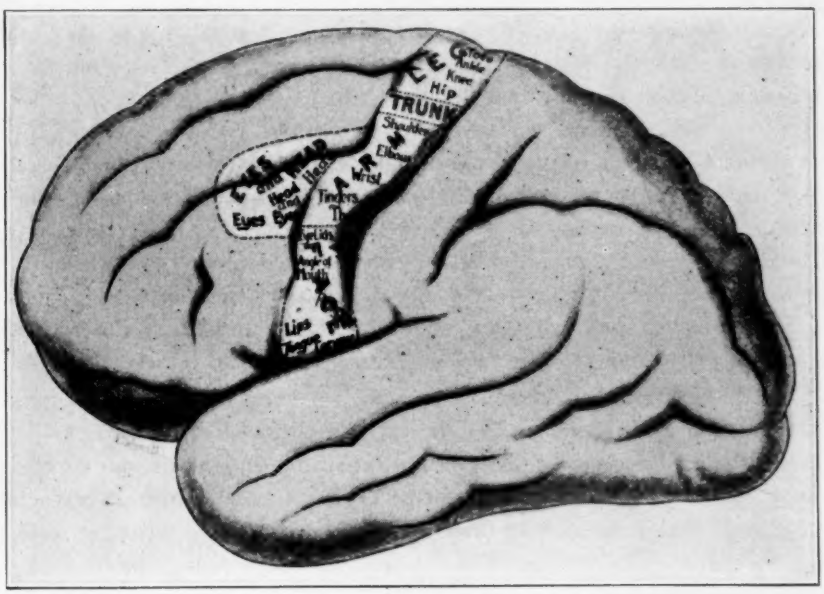


Fig. 9.—Scheme of the motor zone of the human brain published by Mills and Frazier in 1906, on the basis of 10 cases personally studied. However, analysis of these cases (fig. 10) reveals that the data supplied by them were insufficient to justify preparation of the "map" shown in this figure.

Mills and Frazier, however, presented in their paper a schematic drawing of the human brain showing the exact position of the motor centers for the movements of the toes, ankle, knee and hip—all situated on the lateral surface of the brain (fig. 9). The personal observations of these men on the human brain certainly did not warrant this localization (fig. 10); nor, indeed, did any of the cases at that time reported in the literature, as has been pointed out in the preceding part of this historical review.

The inference, therefore, is inescapable that, in placing in their "map" of the human brain primary motor centers for the various parts of the lower extremity on the lateral surface of the cerebral hemisphere, Mills and Frazier must have drawn heavily on the animal experiments of physiologists.

In 1908, Keen's "Surgery" was published, with the section on surgery of the head and brain written by Cushing.[8] In this section there appears a schematic drawing of the human brain showing individual motor centers for the foot, knee and hip on the lateral surface of the cerebral hemisphere (fig. 11). The case of Cushing and Thomas, previously discussed in this paper (table 1, case 59; and table 2, case 4), in which a large, chronic cyst (fig. 7) was removed from beneath the postcentral and precentral gyri, was also reported in the same year. In discussing this case, Cushing stated that "in this patient for the first time, I succeeded in eliciting clean-cut movements of the toes, lower leg and thigh." It seems a reasonable conclusion, therefore, that the positions which he assigned to the motor centers for the leg on the lateral surface of the cerebrum in the schema which he created for Keen's "Surgery" were based on a single personal observation of these centers. Furthermore, this single observation had been made on a brain which harbored a huge subcortical cyst underlying and almost certainly distorting the region under consideration.

In publishing this schema delineating in such detail the positions of the primary motor centers for the various parts of the lower extremity in man, when his personal observations regarding these particular centers were admittedly so limited, one suspects that Cushing must have been "fortified" by his intimate knowledge of Sherrington's authoritative work on the great apes, in which the primary leg centers were found to be situated on the lateral convexity of the cerebrum. These localizations may be compared with those which Cushing reported in 1909 (fig. 12).[7m']

In 1912, Krause,[7n'] of Germany, published in three volumes the comprehensive and beautifully illustrated "Surgery of the Brain and Spinal Cord," an entire volume of which he devoted to the subject of epilepsy. In this extraordinary work, which evidently has been overlooked by some of the more recent writers, Krause reported in great detail his experiences in 13 cases in which he had stimulated the cerebral cortex with electric currents. This investigation was undertaken at a time when, so far as the human brain was concerned, localization of the

8. Keen, W. W.: Surgery: Its Principles and Practice, Philadelphia, W. B. Saunders Company, 1908, vol. 3, pp. 156-157.

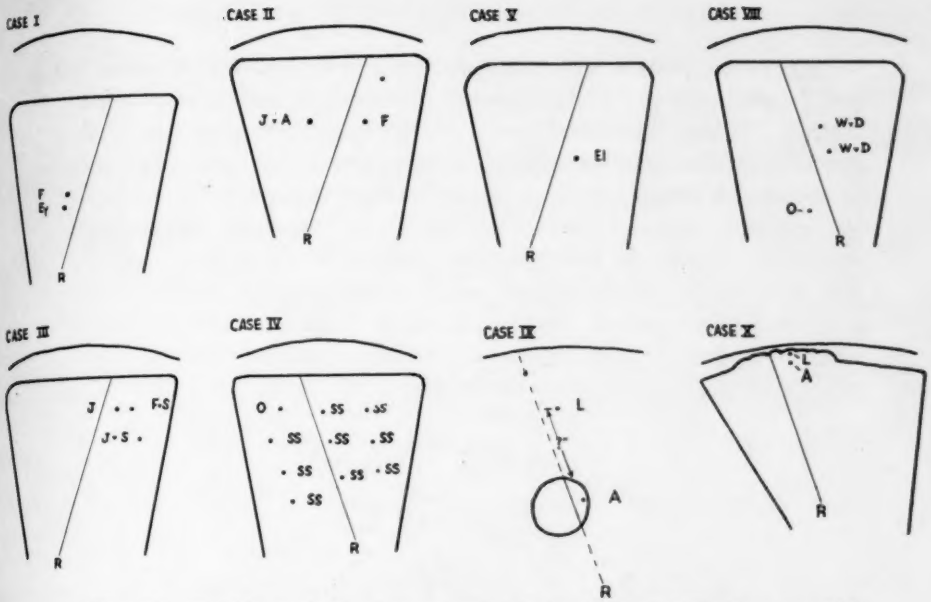


Fig. 10.—Graphic analysis of cases reported by Mills and Frazier on which they based their "map" of the human brain (fig. 9). Compare the paucity of direct observations on the leg centers actually made at the operating table with the elaboration of the "leg centers" on the "map." *R* indicates the rolandic fissure; the area for the face is shown by *F*, for the eyelids by *Ey*, for the jaw by *J*, for the arm by *A*, for the shoulder by *S*, for both shoulders by *SS*, for the elbow by *El*, for the wrist by *W*, for the digits (fingers) by *D*, and for the leg by *L*. The introduction of stimulating electrodes between bone and dura for an unmeasured distance in case 9 is indicated by the symbol *?*

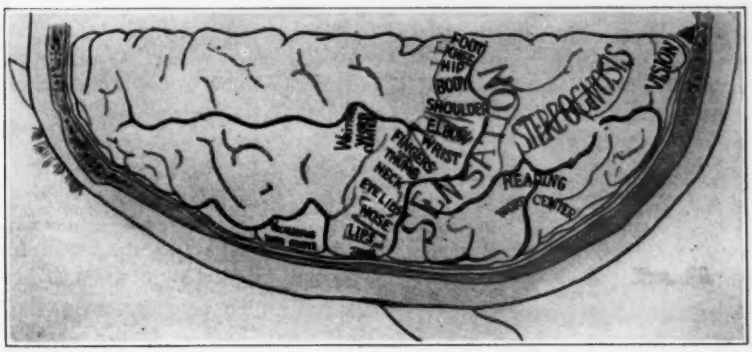


Fig. 11.—The various cortical centers as described by Cushing in Keen's "Surgery" (1908). Evidence indicates that the positions of the leg centers here delineated were based on observations made in a single case in which there was a large subcortical cyst in the parasagittal region (fig. 7). Compare the position marked *elbow* in this diagram with the corresponding area in a later contribution by Cushing (fig. 12).

primary motor centers within the precentral gyrus was still an unsettled and debated subject. It has therefore a historic as well as a physiologic interest. Krause stimulated the brains he studied under well controlled conditions. The points excited were identified and recorded by means of accurate drawings—made in the operating room while the brain was still exposed—many of them in color. Motor responses were carefully described. Finally, in 8 of his cases, portions of the cortex which had thus been studied physiologically were excised and the blocks of tissue given to his colleagues A. Brodmann and H. Vogt for histologic correlation. This fine study, far ahead of its time, is entitled to much greater recognition than it has apparently received.

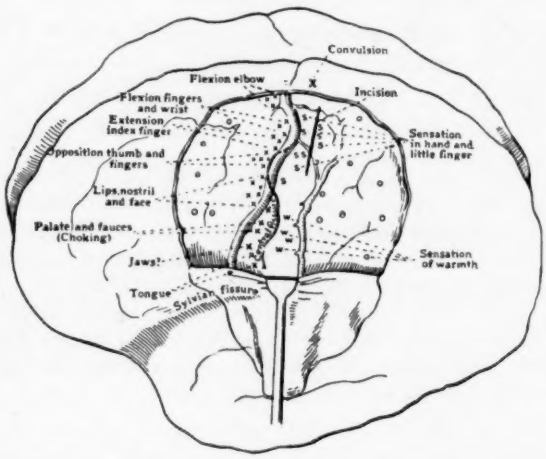


Fig. 12.—The motor and sensory areas as published by Cushing in 1909. Note that the "elbow center" is now placed much nearer the superior mesial border of the hemisphere than in the earlier case of the large subcortical cyst, pictured in figure 11. The localization of 1909 is in agreement with my own observations (fig. 1 *B*).

Krause's actual investigations of the brain were carried out in the most scientific manner. Yet, curiously, one finds that he prepared a "map" of the human brain in which he placed the primary centers for movements of the lower extremity on the lateral surface of the cerebrum, thus totally ignoring his own experimental and operative findings. On the other hand, the map is almost an exact replica of a drawing by Sherrington of the brain of a chimpanzee, to be found conspicuously reproduced on a preceding page of Krause's book.

Study of the individual case reports on which Krause based his "map" of the human cortex discloses not a single instance in which stimulation

of the lateral surface of the cerebral hemisphere produced movements in a lower extremity. On the contrary, in 2 of Krause's cases it seems clear that the cortical centers for movements of the upper extremity extended completely to the superior mesial border, and that the lower extremity was not represented at all on the lateral surface of the hemisphere.

Case 1 in Krause's series illustrates well the point aforementioned. In figure 14 (plate XXVII, Krause [7n']) it will be noted that the upper margin of the

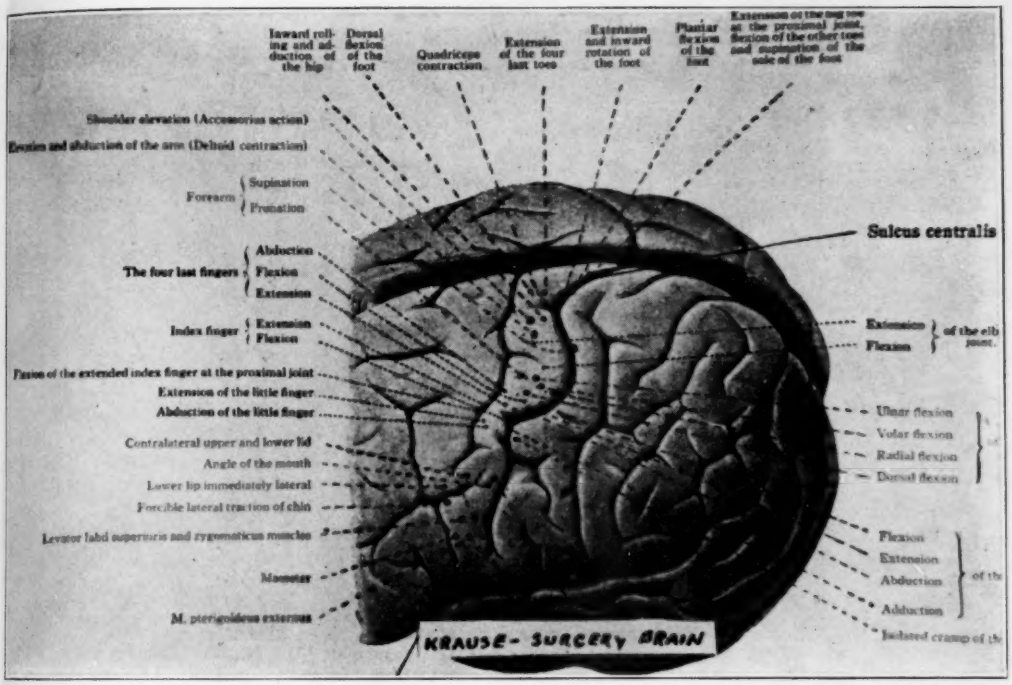


Fig. 13.—Primary motor areas of the human brain as described by Krause in 1910. Observe the minute subdivisions of the area for the lower limb represented here. It is curious, however, that in none of the detailed case reports contained in Krause's volume on epilepsy were movements of the leg elicited by cortical stimulation.

original flap had been extended mesially by rongeurs to a point at the upper lateral border where the large superior anastomotic vein turns to enter the superior longitudinal sinus. Yet stimulation at point *8*, which represents the most superior portion of the lateral hemisphere, produced flexion of the elbow joint! That the motor gyrus was correctly identified is proved by the fact that stimulation of other points on the more lateral and inferior parts of this convolution gave exquisitely focal responses (fig. 14).

Stimulation of *1* gave lateral and downward traction of the left angle of the mouth; of *2*, contralateral innervation of the upper and lower eyelids; of *3*, extension of the index finger and, on further irritation, extension also of the last three fingers; of *4*, radical extension of the wrist joint, followed by flexion of the fingers; of *5*, dorsal flexion of the hand, extension of the two first fingers and inversion of the thumb; of *6*, extension of the thumb separately; of *7*, volar flexion of the wrist, followed by flexion of the second finger, and of *8*, forceful flexion of the elbow joint.

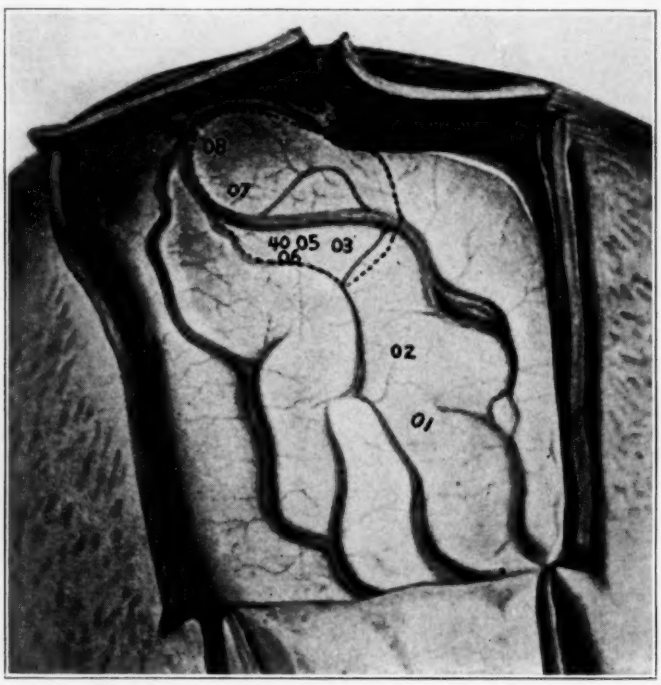


Fig. 14 (plate XXVII).—Krause in this case rongeured away the bone as far as the superior mesial border of the hemisphere, but did not obtain, on stimulation, any movements of the lower extremity. Stimulation of point *8* produced flexion of the elbow. Compare with the preceding figure.

A second case described by Krause (observation I-13), leaves no doubt that the arm area extended completely to the midline and that the leg area was not represented in any way on the lateral surface of this brain. The actual observations were described in part as follows.

After the dura was opened . . . "two veins crossing to the [superior longitudinal] sinus had to be ligated. . . . Unipolar faradization was resorted to. . . . The first contraction was attained at point 1, situated along the sinus longitudinalis superior.

This was characterized by backward movements of the arm and flexor movements of the forearm."

It seems evident from a study of the available material that Krause could not have created his "map" of the human cortex—especially of the leg areas—entirely from his own observations on the human brain. Nor, indeed, could he have done so on the basis of observations then to be found in the literature.

The inference is reasonable, therefore, that in the preparation of his "map" of the human brain, particularly in representing the leg centers in such detail on the lateral surface of the cerebrum, Krause must have been greatly influenced by the observations of physiologists on the brains of animals—especially those of Sherrington and his co-workers on the brains of the great anthropoid apes.

In England, one finds that even Ferrier prepared a "map" of the human brain, which actually was based almost entirely on observations which he had made on the brains of monkeys. In his book, entitled "The Localization of Cerebral Disease," [4d] published in 1879, he pictured a monkey's brain and a human brain, side by side. On the monkey's brain were marked out the same motor points which he had previously described in 1874 (fig. 3).[4a] On the human brain were indicated practically identical motor points. Underneath was this legend: "Upper surface of human brain. The [numbered] circles have the same significance as those on the brain of the monkey."

At the time, however, that Ferrier published his map of the human brain, it is interesting to note there was on record only 1 instance in which the human cortex had been electrically excited. This was the case of Bartholow (table 1, case 1), in which sharp needle electrodes had been plunged directly through a bony defect in the skull caused by an eroding epithelioma of the scalp, and then deeply and blindly into the underlying cortex. Although of considerable historic interest, this case yielded almost no information of scientific value regarding the localization of function in the human brain, except to reconfirm, in a general way, the contralateral representation of function in the hemispheres.

An exact copy of Ferrier's figure showing the motor points on the human brain appeared without modification from 1887 until 1901 in successive editions of a standard English textbook of anatomy. With it went the caption: "Brain of man, showing the localization of various functions (after Ferrier)."

Horsley, on the other hand, successfully resisted temptation to draw up a "map" of the human brain. However, in 1909, in connection with the Linacre lecture,[71] he published a photograph of a hardened brain

on which he had marked out with pen and ink, as accurately as possible, "the few motor points" which he stated he "had personally stimulated in man, together with the responses which they had enlisted." It is noteworthy that on this brain he indicated "motor points" for all parts of the upper extremity and for the hip joint, but not for the knee, ankle or toes.

It is surprising, considering his extensive and classic studies on the localization of motor centers in experimental animals, that Horsley gave so few case reports containing similar observations on the human brain. One such case, however, which he reported in great detail,[71] deserves special mention, since it furnished impressive evidence that the primary motor centers for the lower extremity are not located on the lateral surface of the cerebral cortex.

A boy aged 14 had suffered since the age of 7 from violent athetosis of the entire left upper extremity, involving the shoulder, elbow, wrist and fingers. It was proposed to excise the motor arm area to stop these movements.

On March 20, 1908, to use Horsley's words, "the bone was removed as shown in the accompanying diagram so as to expose completely the Rolandic region" (fig. 15). With use of the faradic current and bipolar electrodes, "the gyrus praecentralis was then thoroughly explored," and the results of stimulation at the points numbered in the accompanying diagram were as follows (fig. 15): *1*, movements of the left side of the face; *2*, abduction of the left thumb; *3*, flexion of the fingers and wrist, with ulnar adduction and late flexion of the elbow; *4*, extension of the fingers, ulnar abduction of the wrist, questionable flexion of the elbow; *5*, extension of the wrist, elbow held at right angles in "confusion" (Beevor and Horsley); *6*, same response as in 5, and, in addition, abduction at the shoulder; *7*, no movements of the upper limb; *8*, elbow held at a right angle, powerful retraction of the shoulder; *9*, elbow at a right angle, retraction of the arm and extension of the wrist; *10*, no response, and *11*, protraction of the arm, elbow held at an obtuse angle, extension of the wrist and questionable extension of the fingers.

No other part of the cortex in the neighborhood responded to stimulations, and no movements of the thorax, hip, leg or toes could be obtained.

The entire gyrus was then excised (fig. 15). The effects of this excision were as follows: Immediately afterward there was complete loss of all voluntary movements of the left upper limb. There was no disturbance of power or sensation in the leg. One year later there was partial recovery of voluntary movements of the left upper limb, that is, abduction of the arm on the shoulder, flexion and extension of the wrist and the fingers. There was no disturbance in the leg, either motor or sensory.

Comment.—Interest in this case centers about the question whether the entire precentral gyrus, situated on the lateral surface of the hemisphere, was exposed by the operative opening, or whether the opening in the bone was so placed that the upper part of the precentral gyrus was not exposed.

In answer to this question there is Horsley's statement that the "bone was removed . . . so as to expose completely the Rolandic region." That this was the case seems to be supported by the operative sketch (fig. 15 left), in which is shown, at the upper border of the bone defect, the large superior cerebral anastomotic veins apparently leaving the

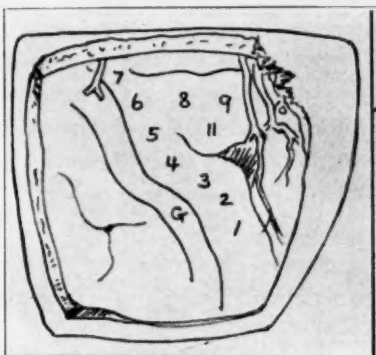


Fig. 4.—Sketch of operation field in case of Hn., made immediately after operation, showing cut edge of bone. Fissure of Rolando or central fissure passes in front of G. The sulcus pre-centralis inferior is shaded. The numbers indicate the points stimulated. (See text.)

Fig. 11.—Outline of the gyrus pre-centralis removed. Abd., abduction; ret., retraction; e.e., elbow extend; w.e., wrist extend; w.f., wrist flexed; ul. ad., ulnar adduction; f.f. fingers flex.

Fig. 12.—Photograph of the gyrus pre-centralis fixed in formol. The scale is that of centimeters and millimeters. The points excitable may be transferred to this figure from Figs. 4 and 11.

Fig. 15.—Horsley reported a case in which he stimulated the entire extent of the precentral gyrus exposed on the lateral convexity of the cerebrum without obtaining motor responses in the lower extremity (top, right and left), and then excised this gyrus (bottom, center) without producing any paresis of the leg. Although the inference would appear inescapable that the primary leg centers are located not on the lateral but on the mesial surface of the hemisphere, Horsley, curiously, denied this.

cortex to enter the superior longitudinal sinus. Moreover, the length of the convolution removed was so great (fig. 15 below) that the excision

must have reached, in its upward extent, close to the midline (fig. 15 below). One would have expected at least partial or temporary paresis of some of the parts of the lower extremities after such extensive removal if the primary motor centers for the lower extremity were really situated on the lateral convexity of the hemisphere.

This case, therefore, contributes strong evidence against the location of the primary leg centers on the lateral surface of the cerebrum, and hence support for their location on the mesial surface—a general truth which Horsley evidently failed to recognize.

All clinical observations regarding the position of the primary motor centers for the lower extremity made directly on the human brain by British surgeons from 1874 to 1914 can be summarized as follows:

1. Bidwell and Sherrington, in 1893, reported a case in which they thought that they had identified the primary "leg center," and excised it, only to find, postoperatively, that the patient had no weakness whatever in the limb in question. It is obvious, therefore, that in this case the primary motor center was not actually located.

2. Horsley, in 1909, reported that he had never been able to elicit primary motor responses in the toes, ankle or knee of any patient by stimulating the lateral surface of the cerebrum with a current of physiologic intensity.

3. Horsley, in 1909, excised, in a boy, all of the precentral gyrus situated on the lateral surface of the cerebrum, without producing any sensory or motor changes in the leg.

Conclusion.—The concept that the primary leg centers in man are situated on the lateral convexity of the cerebrum had already become well established in the current medical journals, and even in the standard textbooks of anatomy, during the period from 1874 to 1914. However, a critical review of the literature leads to the conclusion that this could not have been on the basis of direct observations made on the human brain and, therefore, must have taken place through the gradual acceptance, and transference to the human brain, of data obtained, experimentally, from the brains of animals.

REVIEW OF MORE RECENT LITERATURE (1919-1939)

An anatomic and experimental groundwork for further studies in cortical localization of function was supplied by the preliminary publications and the classic monograph (1919) of Cecile and Oskar Vogt[9] (fig. 16).

9. Vogt, C., and Vogt, O.: Zur Kenntnis der elektrisch erregbaren Hirnrinden-Gebiete bei den Säugetieren, J. f. Psychol. u. Neurol. **8**:277-456, 1906-1907. Vogt, O.: Die myeloarchitektonische Felderung des menschlichen Stirnhirns, ibid. **15**: 221-232, 1909-1910; Die Myelo-architektonik des Iso-Cortex parietalis, ibid. **18**:

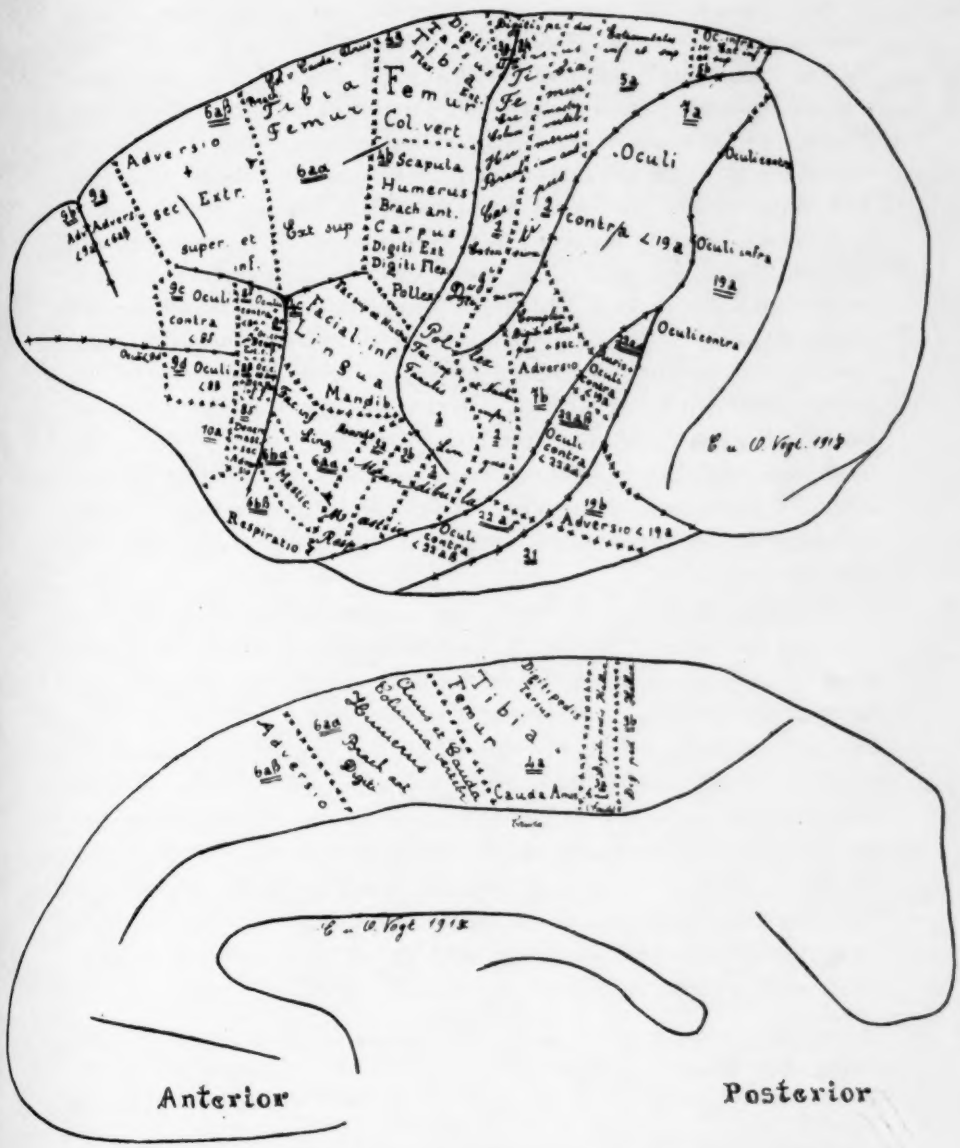


Fig. 16.—An anatomic and experimental groundwork for further studies on cortical localization of function was supplied, in 1919, by the classic monograph of Cecile and Oskar Vogt. These drawings show the various cytoarchitectural and physiologic fields in the long-tailed monkey as described by them.

The contributions of the Vogts were both anatomic and physiologic. The anatomic portion consisted of elaborate cytoarchitectural studies of both primate and human brains; in this connection, these authors were among the first to direct attention not only to the "primary" but to the "secondary" and "tertiary" cortical fields. The physiologic studies consisted of detailed electrical excitation of the cortex of primates. Finally, on the basis of their comparative anatomic studies the Vogts speculated as to the positions which the various physiologic fields they had found in the ape would probably occupy on the brain of man. It is not too much to say that this monumental study, representing as it did the combined efforts of these two brilliant anatomists and physiologists over a period of eleven years, has had an immediate and lasting effect on all subsequent clinical investigations of cortical localization, similar to the influence exercised on clinical thought by the experimental works of Ferrier, Horsley and Sherrington during an earlier period in the study of cerebral physiology.

In man, the chief contributors to the localization of cerebral function since the publication of the Vogts' article in 1919 have been Foerster and Penfield, the latter author working at first with Foerster and later with Boldrey.

Foerster's first contribution to the location of cortical function in man was read before the Breslau Surgical Society in 1924 [10]—five years after the appearance of the Vogts' brilliant monograph. At that time he described primary, secondary and tertiary motor fields in the brain of man, amazingly similar to those which the Vogts had found in the monkey. These observations were published in 1925,[10] the drawing reproduced in figure 18 *A* being the graphic record. Although Foerster has not since made any significant additions or corrections to the *subject matter* reported in the text of his original paper, he has altered considerably the *graphic record* of these observations. For instance, the topographic observations originally published in 1925, as shown in figure 17 *A*, were reported in 1926 as shown in figure 17 *B*.[11]

379-390, 1912. Vogt, C., and Vogt, O.: Allgemeinere Ergebnisse unserer Hirnforschung, ibid. **25** (supp.):279-461, 1919. Vogt, C.; Vogt, O., and Bárány, R.: Zur reizphysiologischen Analyse der kortikalen Augenbewegungen, ibid. **30**:87-121, 1923-1924.

10. Foerster, O.: Zur Pathogenese und chirurgischen Behandlung der Epilepsie (mit Demonstrationen), Zentralbl. f. Chir. **52** (pt. 1):531-549 and 550-558, 1925.

11. Foerster, O.: Zur operative Behandlung der Epilepsie, Deutsche Ztschr. f. Nervenh. **89**:137-147, 1926; Die Pathogenese des epileptischen Krampfenfalles, ibid. **94**:15-58, 1926.

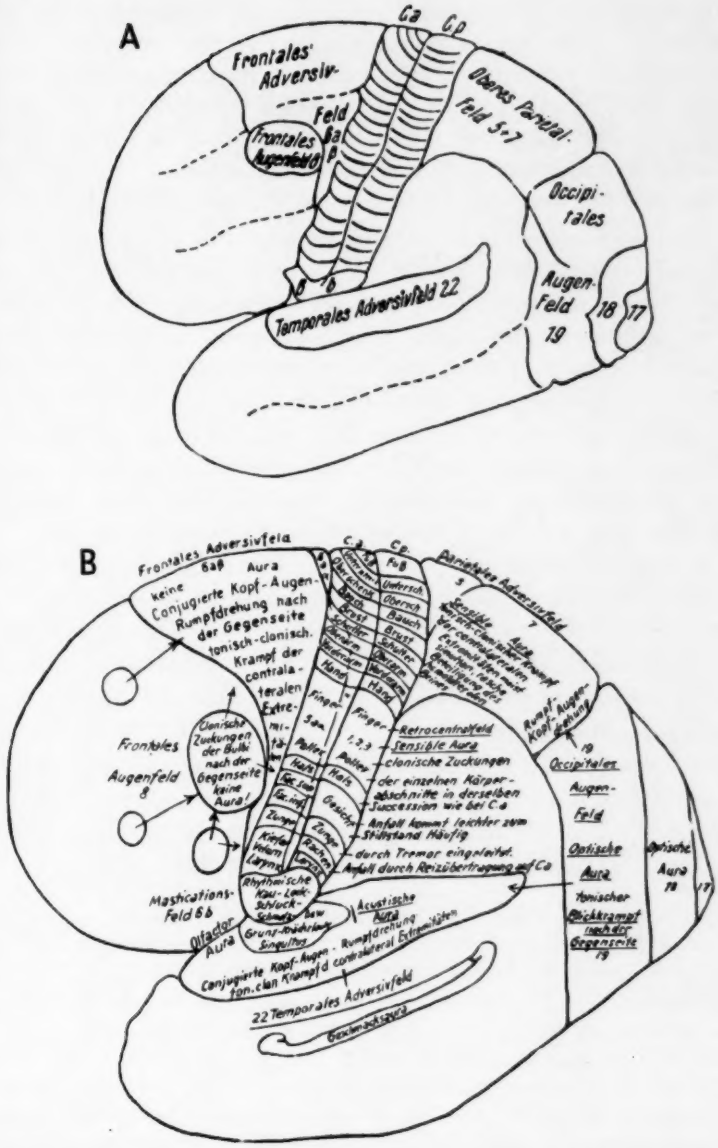


Fig. 17.—Foerster's early charts of the physiologic fields in man. *A*, the illustration accompanying his first article on cerebral localization in 1925; *B*, the various cortical fields mapped by him in 1926.

An article of extreme historical interest was published by the Vogts in 1926.[12] This paper contained several diagrams of the human brain, on one of which they marked out the positions where they believed, on the basis of their comparative histologic studies, that the various physiologic fields which they had identified in the monkey's brain should be found (fig. 18 *A*). On a second diagram of the brain they marked out the positions and forms which they thought to be correct, on the basis of comparative anatomic studies, for the various physiologic fields that Foerster had reported to have found in man (fig. 18 *B*).

Curiously, Foerster seems to have accepted this revision of his own *physiologic* observations, which the Vogts suggested on *anatomic* grounds; and in a lecture delivered in 1931, in London,[13] on the localization of function in the human brain, he used only a copy of this "synthetic" diagram of the Vogts to illustrate his own ten years of experience in the operating room with the exposed human brain. No actual photographs of the operative field and the points of stimulation were used in this lecture, nor have they appeared in any of Foerster's several publications on the subject. This is unfortunate, since they afford the only way by which exact anatomic points on the brain may be precisely recorded and compared; even drawings made from memory shortly after the operation introduce too great an error to be of true scientific value. With only minor variations in drawing, this general schema of the Vogts has been used by Foerster to illustrate all of his subsequent writings on cortical localization of function.[14]

Foerster and Penfield, in 1930,[14a, b] on the basis of 100 of Foerster's cases, published jointly an article reaffirming Foerster's original findings, and summarized them in a chart of the human brain (fig. 19) resembling to a striking degree that suggested by the Vogts. In 1934, and again in 1936, Foerster reaffirmed these original localizations.

---

12. Vogt, C., and Vogt, O.: Die vergleichend-architektonische und die vergleichend-reizphysiologische Felderung der Grosshirnrinde unter besonderer Berücksichtigung der menschlichen, Naturwissenschaften **14**:1190-1194, 1926.

13. Foerster, O.: The Cerebral Cortex in Man, Lancet **2**:309-312, 1931.

14. (*a*) Foerster, O., and Penfield, W.: Der Narbenzug am und im Gehirn bei traumatischer Epilepsie in seiner Bedeutung für das Zustandkommen der Anfälle und für die therapeutische Bekampfung derselben, Ztschr. f. d. ges. Neurol. u. Psychiat. **125**:475-572, 1930; (*b*) The Structural Basis of Traumatic Epilepsy and Results of Radical Operation, Brain **53**:99-120, 1930. (*c*) Penfield, W.: The Radical Treatment of Traumatic Epilepsy and Its Rationale, Canad. M. A. J. **23**: 189-197, 1930. (*d*) Foerster [13]; (*e*) Ueber die Bedeutung und Reichweite des Lokalisationprinzips im Nervensystem, Verhandl. d. deutsch. Gesellsch. f. inn. Med. **46**:117-211, 1934. (*f*) Foerster, O., and Bumke, O.: Handbuch der Neurologie, Berlin, Julius Springer, 1936, vol. 6, p. 50.

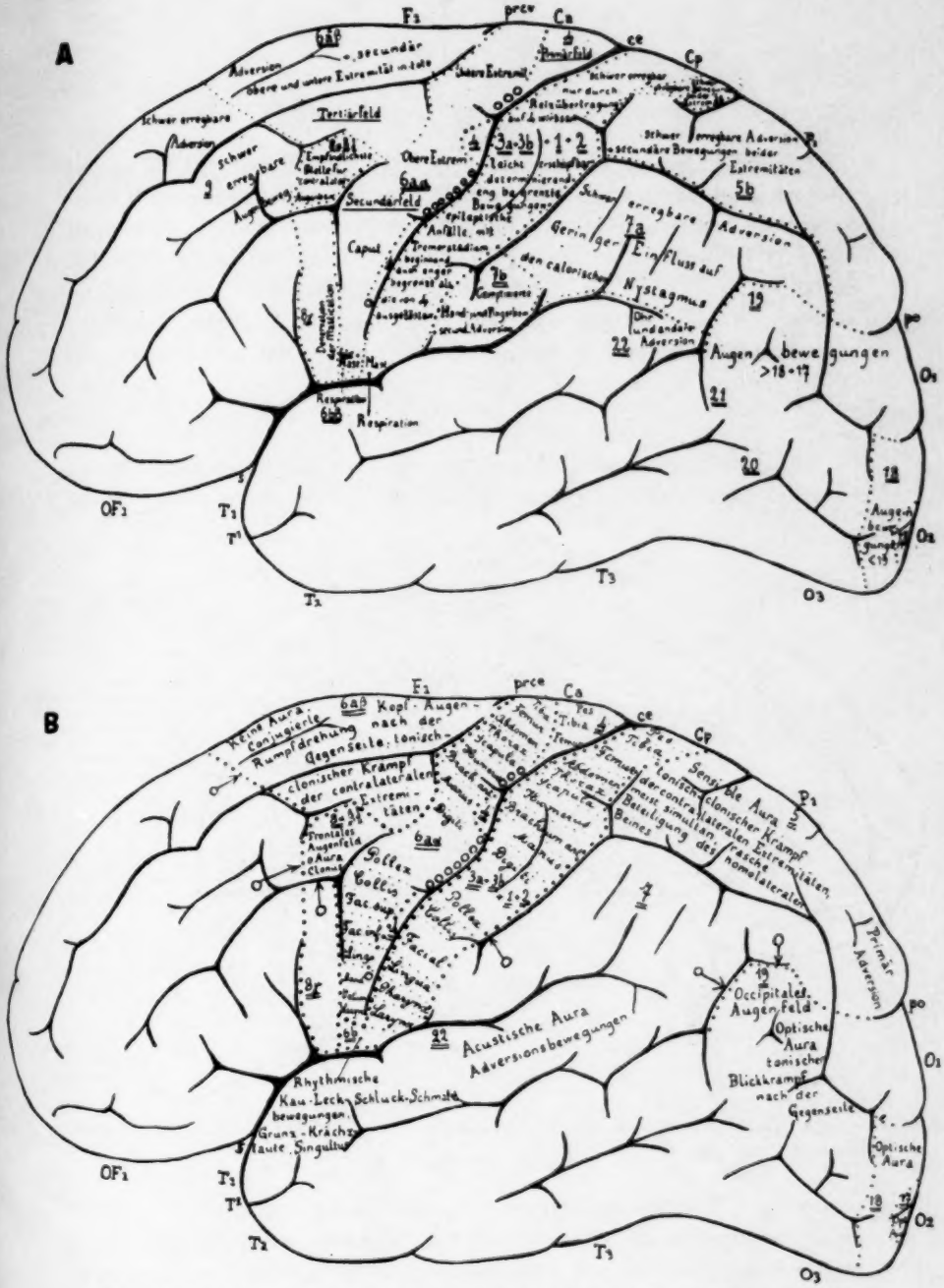


Fig. 18.—Diagrams from a historic article published by Cecile and Oskar Vogt in 1926, in which they suggested, on purely anatomic grounds, an improved pattern for the various "physiologic fields" which Foerster reported to have found. With only minor variations in drawing, the general scheme of the Vogts has been used by Foerster to illustrate all of his subsequent writings on cortical localization.

A, "the human homologue [italics mine] of the architectonic cortical fields of the convexity of the cerebral hemisphere of the long-tailed monkey and their various reactions to physiologic stimulation."

B, "results of stimulating the convexity of the human cerebral hemisphere as mapped out by Foerster prior to 1926, *indicated in schema shown in A* [italics mine]."

Penfield, however, working with Boldrey,[15] published in 1937 results of cortical stimulation (fig. 20) which were at wide variance with those previously reported jointly by himself and Foerster. These differences can best be seen by comparing the "toe area" in figure 19 with that in figure 20 *A*. Despite their serious disagreement in most respects, however, it will be seen that both Foerster and Penfield placed the primary motor centers of the lower extremity on the lateral convexity of the cerebral hemisphere.

ORIGINAL OBSERVATIONS

My own observations differ from those of the other investigators in that I have found the primary motor centers for the upper extremity

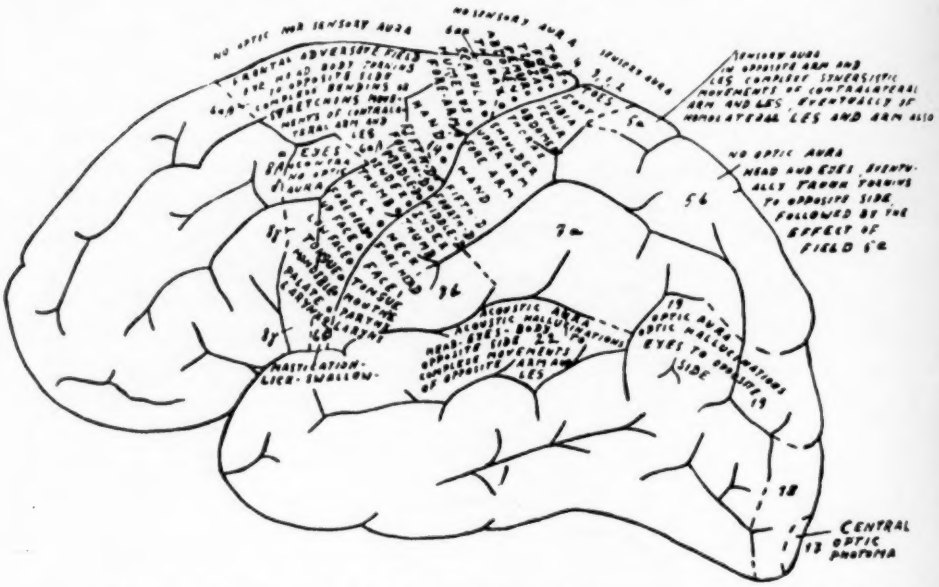


Fig. 19.—Foerster and Penfield's concept of the cortical areas of the human brain in 1930.

commonly to extend upward on the lateral surface of the cerebrum as far as the superior mesial border, and the primary cortical representation for the lower extremity in most instances to be restricted to the mesial surface of the hemisphere.

MATERIAL AND METHODS

The original material presented in this paper consists of 15 consecutive cases in which the superior mesial border of the cerebral hemisphere of man was exposed and electrically stimulated.

15. Penfield, W., and Boldrey, E.: Somatic Motor and Sensory Representation in the Cerebral Cortex of Man as Studied by Electrical Stimulation, Brain **60:** 389-443, 1937.

The patients were all epileptic, with evidence of an irritative focus close to the superior mesial border of the hemisphere. All of them had previously been subjected to encephalographic examination to rule out the presence of tumor and other gross anatomic lesions of the brain capable of producing irritation or distortion. Clinical symptoms and signs are briefly given in the individual case reports.

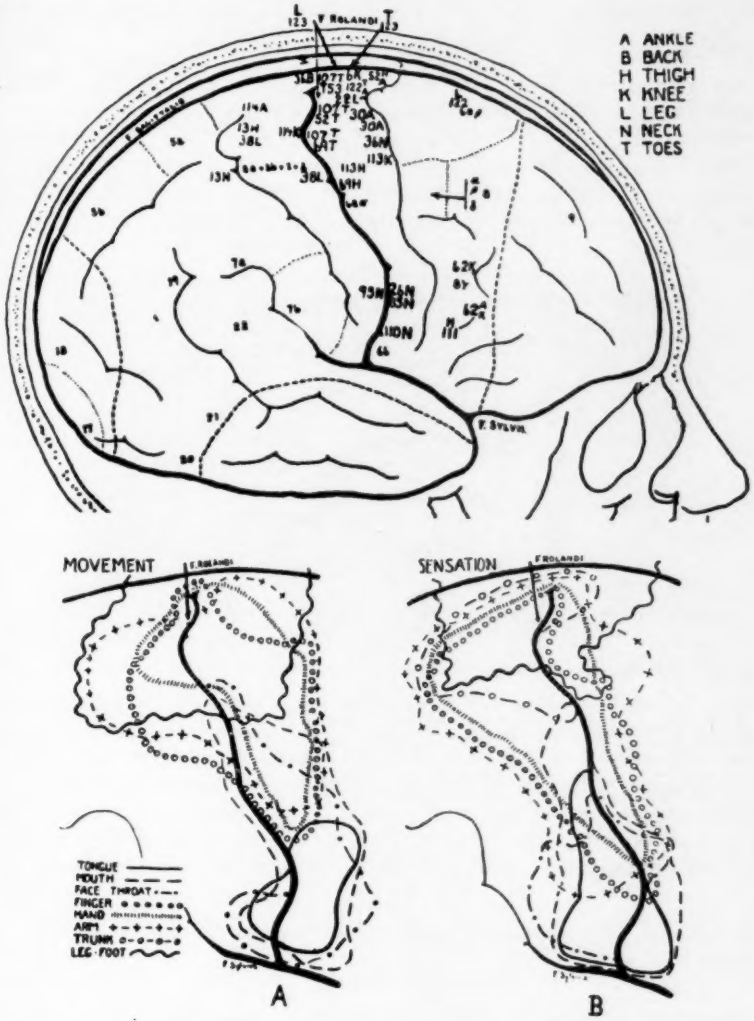


Fig. 20.—Penfield's present concept (1937) of the primary motor cortex for the lower limb. Compare the "toe area" (as shown by the letter *T* in the upper figure) with the corresponding area in the earlier papers published jointly by him and Foerster (fig. 19). Note that in spite of these differences, however, both Foerster and Penfield, and Penfield and Boldrey place the primary motor centers for the lower extremity on the lateral convexity of the cerebrum.

Local anesthesia was used in most instances. In some cases local anesthesia was supplemented with anesthesia induced by avertin with amylene hydrate, and in only 1 instance, that of an infant, was primary ether anesthesia used.

Stimulation was made with faradic current in each instance. A bipolar electrode was used with the points about 3 mm. apart. In some instances the current was obtained from an ordinary induction coil, and in others, from a thyratron equipped with a cathode ray oscillograph. Stimulation of the cortex was always begun with the current just strong enough to produce the smallest visible contraction of a few fasciculi of the exposed temporal muscle. This current was found to be one which, in most instances, would give sharply focal, tonic contractions of individual fingers on stimulation of the motor gyrus of the brain.

The points stimulated were usually recorded by means of sketches made by the operator—necessarily somewhat schematic, but essentially accurate in their important features—and also by photographs. The photographs, in the absence of

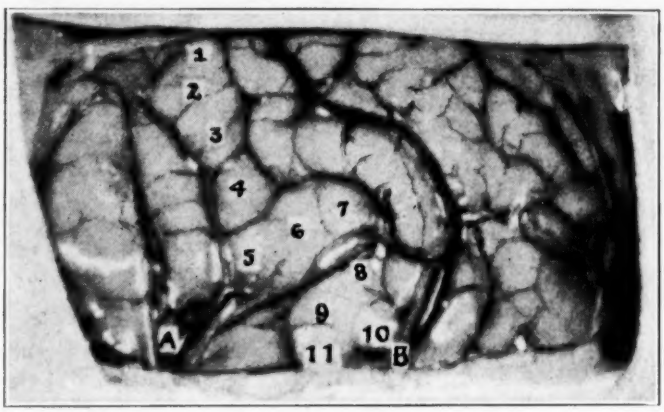


Fig. 21 (case 1).—Response to stimulation: *1*, closure of jaw; *2*, twitching of mouth and chin; *3*, opening of eyelids; *4*, no response; *5*, flexion of terminal phalanx of thumb; *6*, slight flexion of thumb and fingers; *7*, flexion of fingers and wrist; *8*, flexion of forearm; *9*, extension of elbow; *10*, flexion of forearm, pronation and slight movement at shoulder joint; *11*, movements of arm and shoulder and of shoulder alone. Marker *11* is touching the superior longitudinal sinus. *A* and *B* indicate superior anastomosing veins entering the superior longitudinal sinus.

better facilities, were all taken with a "candid" camera by various volunteers on the house staff.

REPORT OF CASES

CASE 1.—E. M., a girl, aged 17 years, was admitted to the Neurological Institute, of New York, on Feb. 2, 1938, with the chief complaint of convulsive seizures affecting principally the left leg, which began in August 1935, approximately two and a half years before.

Examination.—There were slight hypoplasia of the left lower extremity, involving both the skeleton and the muscles, and very slight weakness of the left leg as compared with the right, brought out particularly in dorsiflexion of the

toes. The deep reflexes were slightly more active in the left lower extremity than in the right. The Babinski sign was equivocal on the right. Sensory examination gave normal results. The cranial nerves were normal. The patient was normal mentally.

Laboratory examinations gave essentially normal results.

Roentgenograms of the skull were normal. An encephalogram was normal.

Operation.—On March 2, 1938, right frontoparietal osteoplastic craniotomy was performed. The dura was not tense; when it was opened, the cortex appeared essentially normal.

Stimulation of Right Cortex with the Thyratron Esthesiometer (Local Anesthesia).—Faradic stimulation of the motor cortex was carried out with bipolar electrodes, the points of which were placed 3 mm. apart. The following motor points were identified (fig. 21):

Frequency	Milliamperes Recorded on Cathode Ray Oscillograph	Area Stimulated for Motor Responses	Response
100	16	1	None
	21	1	Closure of jaw
	21	2	Twitching of left side of mouth and chin
	21	2	Clonic contraction of eyelids and sternocleidomastoid muscle; left eye turned to left momentarily
	16	2	No response
	16	3	No response
	16	3	Eyelids opened; voluntarily (?)
	21	3	Eyelids elevated
	21	3	Eyelids opening
	16	4	No response
	21	4	No response
	21	4	No response
	12	5	No response
100	14	5	Flexion of thumb, terminal phalanx
	16	5	No response
	18	5	Flexion of fingers and wrist
	21	5	Flexion (strong) of forearm, wrist and thumb
100	12	6	Thumb and fingers flexed slightly
	12	6	Extension of forearm at elbow; some flexion of wrist; adduction of thumb, and flexion of thumb and index finger
	12	7	Flexion of fingers and wrist
	12	7	Pronation of forearm; flexion of thumb
	7	7	Patient said finger moved, but no visible motion
	16	8	Marked flexion of forearm
	12	8	Flexion of forearm and adduction of thumb
	12	9	Extension of forearm; faint brachioradialis (?) reflex
	12	9	Extension of arm on shoulder, forward movement
	12	9	No response
	21	9	No response
	12	10	Flexion of forearm; pronation; slight movement of shoulder joint
	12	10	Flexion of forearm
	21	10	Pectoral muscles come into action with whole arm; flexion of arm, including shoulder
	12	11	Movement of shoulder
	21	11	Movement of shoulder and arm

Point E is 0.5 cm. mesial to number *11* and is the cortical attachment of a pacchionian granulation which has been divided. Stimulation of a point just anterior to the marker E (at the site of junction of the lateral and the medial border, in an area of divided pacchionian granulation) produced aura. Stimulation of this point produced pain, but no movements of the left foot.

Point F is the other attachment of pacchionian granules on the mesial surface. Stimulation of this point produced a convulsion of the entire left side (especially the arm).

CASE 2.—V. L., a woman aged 23, who was admitted to the Neurological Institute on March 1, 1938, had been run over by a bicycle at the age of 4 and received a depressed fracture in the right frontal region of the skull laterally. Three months before admission she began to have generalized convulsive attacks with loss of consciousness, but without focal features. She had had since a convulsive attack every one or two weeks, and occasionally as many as four attacks in one day.

Examination.—This revealed a depression in the bone, 1.5 cm. in diameter and 0.5 cm. deep, at the junction of the forehead and the right temple with the skin drawn into the depression. There was questionable weakness of the left lower portion of the face. Mentally, the patient was apparently normal.

Laboratory examination gave normal results.

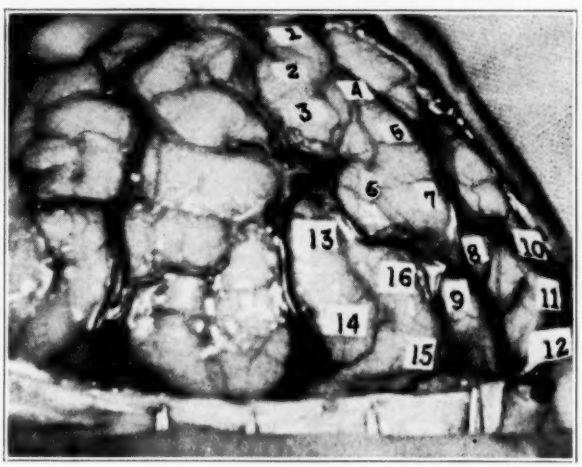


Fig. 22 (case 2).—Response to stimulation: *1*, closure of jaw; *2*, movements of lips, swallowing; *3*, movements of lips and jaw; *4*, opening of jaw; *5*, closing of lips; *6*, movements of lips; *7*, movements of eyelids and eyeballs; *8*, flexion of fingers and clonic movements of fingers, hand, forearm and jaw; *9*, flexion of thumb and index finger; *10*, flexion of wrist, forearm and shoulder and clonic movements; *11*, extension of fingers and flexion of forearm; *12*, flexion of elbow and wrist, partial extension of fingers, clonus spreading to knee, lasting forty seconds. No initial responses were obtained in lower extremity on repeated stimulation of any part of exposed cortex.

Roentgenograms showed a small, old depressed fracture of the right frontal region of the skull. Encephalograms showed mild porencephaly of the right frontal region, associated with slight arachnoiditis.

Operation.—On March 8, 1938, right transfrontal craniotomy (Frazier type) was performed under local anesthesia. When the flap was turned up there was seen an irregular spicule of bone in the middle of the frontal region, apparently protruding into the brain itself. When the dura was opened there was found a marked depression in the surface of the brain beneath the bony spicule, with gliosis and formation of scar tissue about it.

Electrical Stimulation of the Cortex.—With the use of a bipolar electrode and the thyratron, the following motor points were identified (fig. 22):

Area Stimulated	Response
1	Closure of jaw
2	Closure of jaw and lips
3	Jaws and lower lip
4	Opening of jaws and upper lip
5	Closing of lips; twitching
6	Lower lip
7	Eyelids open, then flickering of eyelids
8	Flexion and clonic movements of hand, fingers, forearm and jaw, continued for some seconds
9	Flexion of thumb and first finger
10	Flexion of shoulder, wrist and forearm; clonic movements
11	Flexion of forearm; extension of fingers
12	Flexion of elbow and wrist; partial extension of fingers; clonus of knee; clonic convulsion lasting 40 seconds
13-29	No response obtained on stimulation

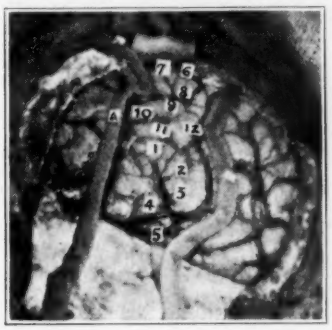


Fig. 23 (case 3).—Response to stimulation: *1*, flexion of fingers; *2*, flexion of fingers and wrist; *3*, pronation of forearm; *4*, flexion of forearm, slight elevation of shoulder; *5*, abduction of shoulder.

Case 3.—A. P., a man aged 21, who was admitted to the Neurological Institute on Jan. 27, 1938, had had his first convulsive seizure in December 1935, two years before admission to the hospital, at which time his eyes rolled upward, his head turned to the left, and he rotated to the left and fell to the floor. This was followed by generalized moderate clonic movements. Since then he had had attacks at intervals of about every two weeks. In all these seizures there were turning of the head and rotation of the body to the left.

Examination.—Neurologic tests gave normal results.

Laboratory findings were normal. Roentgenograms of the skull were normal. Encephalograms showed slight cerebral hypoplasia or atrophy on the right.

Operation.—On Feb. 9, 1938, a right frontotemporoparietal flap was turned up, under local anesthesia. The dura appeared normal and under no increase of tension. When the dura was opened, the cortex presented a normal appearance.

Electrical Stimulation of the Cortex.—A bipolar electrode was used, with current from a faradic induction coil. The current used was just strong enough

to cause the slightest contractions of single fasciculi in the temporal muscles The points stimulated and responses obtained were as follows (fig. 23):

Area Stimulated	Response
6	Movements of left side of the face
8	Movements of left side of the face
1	Flexion of fingers
2	Flexion of fingers and wrist
3	Pronation of forearm
4	Flexion of forearm and elevation of shoulder
5a	Abduction of shoulder
Point stimulated just anterior to marker 5	
5b	Quick simultaneous movement of arm and ankle
Point stimulated just posterior to marker 5; this point probably corresponds to area 5a of Vogt	
Stimulation of the premotor area	No motor responses elicited

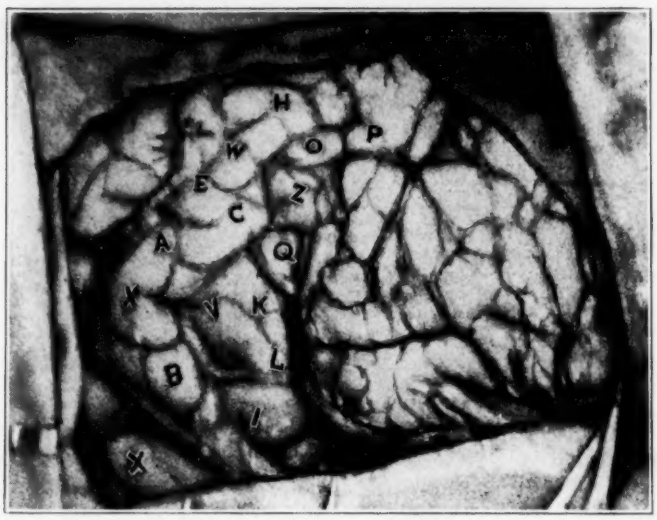


Fig. 24 (case 4).—Response to stimulation: *K*, flexion of fingers and pronation of forearm; *L*, flexion of forearm at elbow; *I*, extension of forearm and slight elevation of shoulder. No movement of the lower extremity could be elicited. The clamps are on the edge of the superior longitudinal sinus.

Case 4.—C. W., a man aged 20, was admitted to the Neurological Institute on March 29, 1938, complaining of generalized convulsive seizures, accompanied by loss of consciousness and urinary incontinence, but without focal features; they had been recurring since October 1933.

Examination.—Neurologic examination gave essentially negative results.

Laboratory examinations all gave results within normal limits. The total protein of the spinal fluid was 34 mg. per hundred cubic centimeters.

Roentgenograms of the head were normal. Encephalograms showed mild left cerebral atrophy.

Operation.—On May 21, 1938, a left frontoparietal flap was turned up. The convolutions appeared normal, and no atrophy or neoplasm was observed.

Cortical Stimulation.—With use of a bipolar electrode and current from the thyratron, the following motor points were identified (fig. 24):

Area Stimulated	Response
B	Flexion of elbow, wrist and fingers
K	Flexion of fingers and pronation of forearm
K	Flexion of wrist and pronation of forearm
L	Flexion of forearm and arm
I	Abduction of arm (deltoid) and slight elevation of shoulder
I	Elevation of shoulder, slight abduction of arm (trapezius and deltoid)
Q	Abduction of wrist and flexion of fingers
L	Flexion of forearm
I	Shoulder (deltoid and trapezius)
I	Elevation of shoulder and extension of forearm

CASE 5.—F. A., a boy, aged 15, was admitted to the Neurological Institute on May 17, 1938, because of severe jacksonian convulsions on the right side, which had begun in March 1933. The patient was mentally retarded.

Examination.—Physical examination revealed a normal appearance. There was no gross motor weakness. However, the automatic associated movements of the

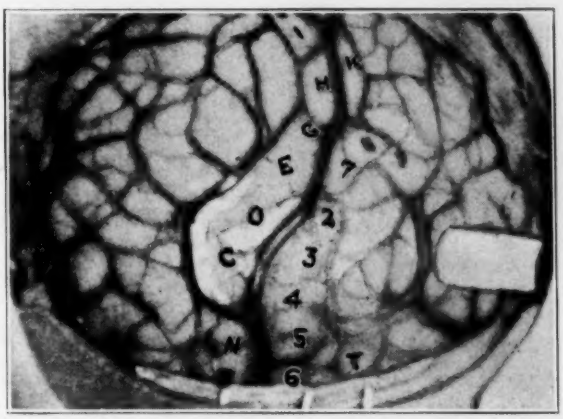


Fig. 25 (case 5).—Response to stimulation: *3*, flexion of fingers; *4*, partial flexion of wrist; *5*, extension of wrist, *6*, elevation of shoulder.

The tips of the clamps shown are on the edge of the superior longitudinal sinus.

right arm were suppressed, and the right arm and hand were slightly smaller than the left. There was also some dysmetria in performing the finger to nose tests with the right hand. The reflexes were slightly exaggerated on the right side, particularly in the lower extremity; plantar flexion was not as active in the right foot as in the left. Slight weakness of the right lower part of the face was noted. There was slight hesitation in speech.

Laboratory examinations revealed nothing unusual.

Roentgenograms of the head were normal. Encephalograms revealed mild atrophy of the left side of the brain.

Operation.—On June 6, 1938 a left frontoparietal bone flap was turned up. The brain was not tense, and nothing abnormal was seen on inspection.

Cortical Stimulation.—This was carried out, with the following results (fig. 25):

Area Stimulated	Response
2	No response
3	Flexion of fingers and partial flexion of hand
4	Partial flexion of wrist and extension of fingers
5	Extension of wrist and flexion of fingers; anterior rotation of shoulder
6	Slight adduction of forearm and elevation of shoulder

Case 6.—B. L., a Jewish woman aged 35, who was admitted to the Neurological Institute on July 5, 1938, had suffered violent trauma to her head in 1916. About six months later she experienced her first convulsive attack, and attacks had recurred ever since. The seizures were preceded by a sensation of "jerking," or twitching, in the right antecubital fossa, without, however, any coincident objective muscular movements. During this time, however, the patient was unable to continue any motion that might have been in progress at the time that the peculiar jerking sensation started. Within a few seconds after this subjective phenomenon, there developed a typical grand mal seizure without definite focalization, or even lateralization, of motor phenomena.

Examination.—Neurologic examination gave normal results except for slight suppression of automatic associated movements of the right upper extremity on

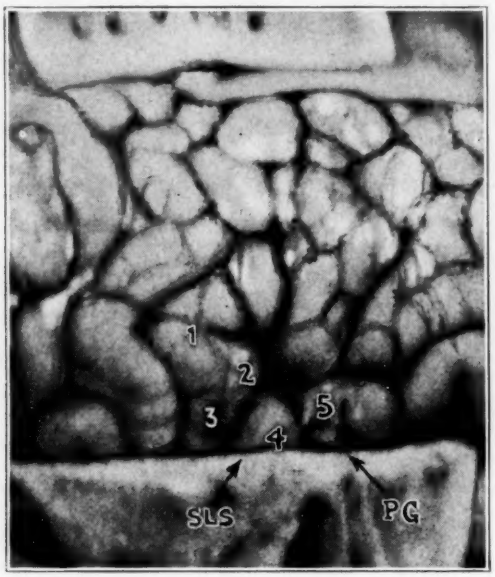


Fig. 26 (case 6).—Response to stimulation: *1*, flexion of fingers; *3*, flexion of elbow; *4*, generalized convulsions; *SLS*, superior longitudinal sinus; *PG*, pacchionian granulation.

walking, and slight weakness of the right lower part of the face on emotional stimulation.

Laboratory examinations all gave normal results.

Roentgenograms of the head were normal. Encephalograms revealed nothing abnormal.

Operation.—On July 27, 1938, a left frontoparietal osteoplastic flap was turned up, extending just across the midline. In doing so, the superior longitudinal sinus was torn with brisk bleeding for a time, followed by an alarming fall in blood pressure. The patient was immediately given a blood transfusion, but the blood pressure did not return to its original level, and her condition following this hemorrhage was not reassuring.

Cortical Stimulation.—Because of the poor condition of the patient, extensive electrical exploration of the cortex was not carried out, the operator contenting himself with a limited number of observations identifying the motor gyrus. The results of these stimulations are given here (fig. 26):

Area Stimulated	Responses
1	Flexion of fingers
3	Flexion of right elbow
4	Generalized convulsions

CASE 7.—J. B., a man aged 22, an alert, affable Pole, was admitted to the Neurological Institute on March 31, 1938, suffering from both grand and petit mal attacks, of eight years' duration. The attacks started with twitching of the left side of the face and turning of the eyes toward the left, followed by clonic

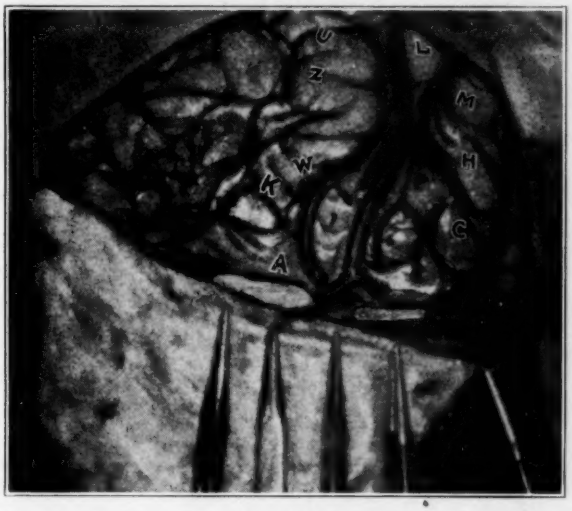


Fig. 27 (case 7).—Response to stimulation: *K*, extension of fingers; *A*, flexion of arm at elbow. The superior anastomosing veins have already been divided. The cotton pledgets separate the superior mesial border of the hemisphere from the superior longitudinal sinus and the falx.

movements of the left arm, which quickly spread to involve all the other extremities. There was coma, lasting a few minutes.

Examination.—Neurologic examination gave entirely normal results.

Laboratory examination revealed nothing abnormal The total protein of the spinal fluid was 18 mg. per hundred cubic centimeters. Serologic reactions were normal.

Plain roentgenograms showed changes in the skull such as might be associated with left cerebral hypoplasia. Encephalograms revealed mild bilateral cerebral atrophy, slightly more marked on the left side.

Operation.—On May 5, 1938, a right frontoparietal osteoplastic flap was turned up. The cortical markings appeared to be essentially normal. Two superior anastomosing cerebral veins, passing from the cortex to the superior longitudinal sinus, appeared to be of unusual size.

Cortical Stimulation.—The following responses were obtained (fig. 27):

Area Stimulated	Response
U	Mandible pulled down
Z	Left eyebrow raised
W	Extension of hand
A	Flexion of arm at elbow
K	Extension of fingers
Premotor area	Entire premotor area stimulated; no objective response until pacchionian granulations in premotor area were approached; then the following responses were obtained: flexion of left elbow, clonus of right side of face, flexion of left elbow, extension of left shoulder

Case 8.—J. H., a woman aged 32, who was admitted to the Neurological Institute on Nov. 23, 1937, twenty-five years before had been found under a table, unconscious, and had remained so for ten or fifteen minutes. About a year later she had her first generalized convulsion. Similar convulsions had occurred since, and constituted her chief complaint. There had been no focal features of the

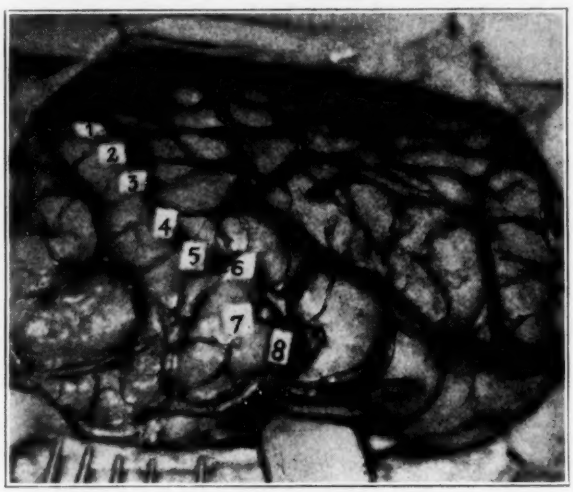


Fig. 28 (case 8).—Response to stimulation; *5*, movements of jaw; *6*, movements of thumb and index finger; *7*, flexion of fingers and wrist; *8*, flexion of elbow. Marker *8* is at the superior mesial border of the hemisphere. The large superior anastomosing vein has been divided, and the cortex has been lifted away from the superior longitudinal sinus and the falx by cotton pledgets. The clamps are on the lateral edge of the sinus, pulling it down to expose the falx.

convulsions themselves, except possibly for initial turning of the head to the left. The attacks had increased in frequency until they occurred about every two weeks, and might come at any time of the day or night. In June 1936, there developed weakness of the left arm and leg. There had been considerable mental slowing during the past few years.

Examination.—The patient was of subnormal intellect, with left hemiparesis, involving particularly the arm. There was accompanying hyperreflexia on the left side. Muscle tendon sense was markedly reduced in the fingers of the left hand. There were weakness and hypesthesia of the left side of the face and left homonymous hemianopia.

Laboratory examinations were essentially normal. The total protein of the spinal fluid was 18 mg. per hundred cubic centimeters. Serologic reactions were negative.

Plain roentgenograms of the skull showed slight asymmetry of the cerebrum, probably congenital. Encephalograms showed cerebral hypoplasia with porencephaly on the right side, involving the parietal and occipital lobes.

Operation.—A right parieto-occipital bone flap was turned up on Dec. 17, 1937. This revealed marked atrophy and gliosis of the parietal and occipital lobes, which were later excised.

Electrical Stimulation.—The following results were recorded (fig. 28):

Area Stimulated	Response
1	No response
2	No response
3	No response
4	No response
5	Movements of jaw
6	Movements of thumb and index finger
7	Flexion of fingers and wrist
8	Flexion of elbow

Although stimulation was applied to the rest of the exposed cortex, no motor responses were obtained.

CASE 9.—A. M. B., a girl aged 14, was admitted to the Neurological Institute on Nov. 12, 1938, with the history that since the age of 2½ years she had been suffering from convulsions, involving chiefly the left arm and leg. During the past seven and a half years, however, the spells had become generalized.

Examination.—The patient was emaciated and in status epilepticus. Under intensive sedation the convulsions became less frequent and less severe, when it was definitely established that the attacks actually began on the left side of the body.

Laboratory examinations gave essentially normal results.

Roentgenograms of the skull were normal. Encephalograms revealed left hypoplasia, of slight degree.

Operation.—On Nov. 1, 1938, a right frontoparietal osteoplastic flap was turned up with the use of local anesthesia supplemented by avertin with amylene hydrate. The dura was not tense and was opened widely. There was no bulging of the brain. The convolutions appeared normal. Several unusually large veins ran across the cortex to converge near the superior mesial border before entering the superior longitudinal sinus in a single large vessel.

Electrcial Stimulation.—The following motor points were identified (fig. 29):

Area Stimulated	Response
1	No response
2	No response
3	No response
4	Movements of thumb and index finger
5	Flexion of fingers and wrist
6	Flexion of elbow
7	Elevation of shoulder
After Division of Pacchionian Granulations Mesial to 7:	
C	Movement of shoulder
D	Slight twitching of toes

CASE 10.—H. J., a boy aged 18 months, was admitted to the Neurological Institute on Oct. 27, 1938, because of jacksonian convulsions, of considerable severity, starting in the right arm and associated with right hemiparesis, which came on during a febrile illness at the age of 15 months. They occurred as often as ten or fifteen times a day.

Examination.—There was right spastic hemiparesis. The child was willing to attempt to walk, although he frequently fell in doing so. He did not speak spontaneously. However, he understood simple commands and was cheerful, active and playful.

Laboratory examinations gave normal results.

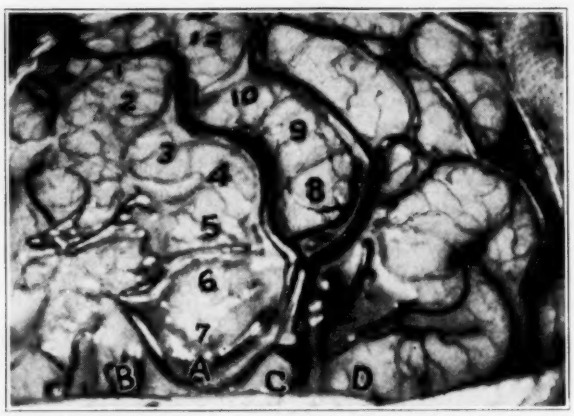


Fig. 29 (case 9).—Response to stimulation: *4*, movement of thumb and index finger; *5*, flexion of fingers and wrist; *6*, flexion of elbow; *7*, elevation of shoulder; *C*, movement of the shoulder. The tips of the mosquito clamps just showing at the lower edge of the photograph are on the edge of the superior longitudinal sinus.

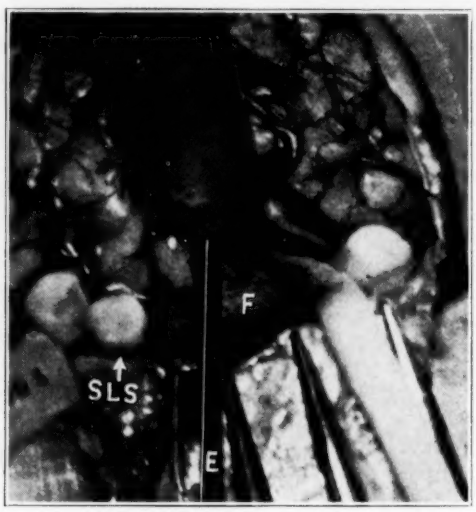


Fig. 30 (case 10).—Retraction of the cerebrum from the falx and stimulation of its mesial surface. The superior longitudinal sinus (*SLS*) is pulled downward by mosquito clamps attached to its lateral border. The falx (*F*) is plainly visible. Stimulation with the electrode (*E*) at a point about 1 cm. beneath the superior mesial border elicited movements in the foot and ankle. Stimulation at a point about 2 cm. beneath the border of the hemisphere (gyrus cinguli) produced focal contractions of the rectal sphincter, without other discernible motor responses.

Roentgenograms of the skull were nomal. Encephalograms revealed generalized cerebral atrophy.

Operation.—A left parietal craniotomy was performed on Nov. 11, 1938. The brain was not under tension. Convolutional markings were not abnormal.

Cortical Stimulation.—Stimulation of the lateral surface of the hemisphere elicited focal movements of the wrist, elbow and shoulder, but not of the lower extremity. Two of the large superior anastomosing veins were then doubly ligated and the pacchionian granules separated, and stimulation of the mesial surface of the hemisphere was carried out (fig. 30).

Stimulation of the mesial surface from the superior border downward for a distance of about 1.5 cm. produced various movements of the lower extremity.

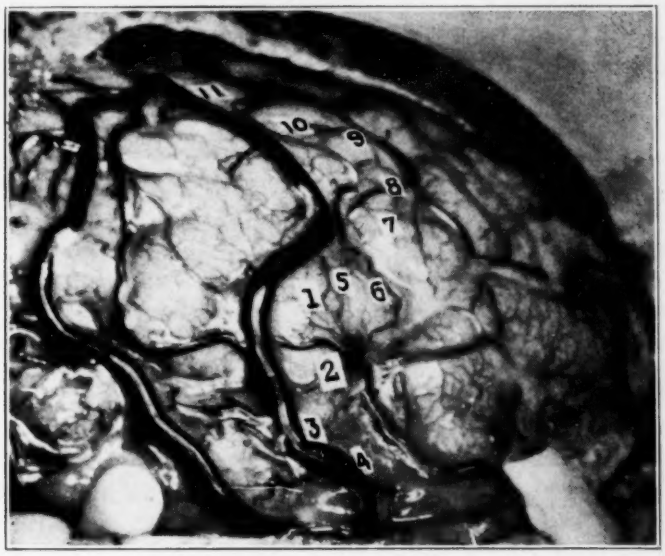


Fig. 31 (case 11).—Response to stimulation: *1*, flexion of elbow; *2*, elevation of shoulder; *3*, elevation of shoulder; *4*, contraction of right rectus muscle. No motor responses were obtained in the lower extremity. The large superior anastomosing veins can be seen entering the sinus.

Stimulation in an area about halfway between the superior border and the corpus callosum and extending farther downward toward the corpus callosum produced sharply focal contractions of the rectal sphincter. These contractions, observed by Dr. Jean Sirois by placing his finger within the rectum, were sharp, immediate and focal, and were not accompanied by movements of the lower extremity. Tests were repeated several times to assure the accuracy of the observation.

Case 11.—St. C. C., a Negro boy aged 16, was admitted to the Neurological Institute on Nov. 17, 1938, suffering from jacksonian seizures on the right side. In November 1935 he had been knocked unconscious for a half-hour in a boxing match, but after return to consciousness he took part in fifteen more bouts. In

the spring of 1936 the patient experienced his first convulsion. Since then episodes had occurred about once a month.

Examination.—Marked suppression of the automatic associated movements of the right arm, together with marked reduction in the "check element" in the same extremity, was revealed. There was an equivocal Babinski sign on the right side, as opposed to a good plantar response on the left. Otherwise, examination gave normal results.

Laboratory examinations revealed nothing unusual.

Roentgenograms were normal. Encephalograms revealed mild, diffuse cerebral hypoplasia.

Operation.—On Dec. 3, 1938, a left parietal bone flap was turned up under local anesthesia. The brain was not tense, and the convolutions themselves had a normal appearance. There was, however, more subarachnoid fluid than usual.

Electrical Stimulation of the Cortex.—This was carried out, with identification of the following motor points (fig. 31):

Point on Motor Cortex	Response
1	Flexion of forearm
2	Raising and drawing back of right shoulder
3	Raising and drawing back of right shoulder
4	Contraction of right lower rectus muscle
Point just medial to 4	Contraction of right lower rectus muscle
5	Abduction of thumb
5	Abduction of hand
6	Abduction of thumb
7	Seizure first involving right arm, then becoming generalized

CASE 12.—S. F., a man aged 20, was admitted to the Neurological Institute on May 5, 1937, because of jacksonian convulsions starting in the left arm, which had begun in the first year of life. In spite of 10 grains (0.65 Gm.) of phenobarbital a day, he had a major attack about twice a week.

Examination—The results were entirely normal.

Laboratory examinations all gave findings within normal limits.

Operation.—On May 6, 1937, a right frontoparietal osteoplastic flap, which exposed the superior longitudinal sinus and the superior mesial edge of the hemisphere, was turned up without difficulty.

Photographs of the brain were taken at this time, with the various points of stimulation identified by numbers. Unfortunately, however, this is the first of 3 cases (see cases 13 and 14) in which the films were lost, so that a picture of the brain cannot be reproduced.

Stimulation of Right Cortex with the Thyratron Esthesiometer (Procaine Anesthesia).—The important point in the record is that the pacchionian granulations along the superior mesial border of the hemisphere were divided, together with the superior anastomosing veins, and that electrical stimulation was carried out right up to the mesial surface of the hemisphere without obtaining any responses from the lower extremity.

Area Stimulated	Amperage	Voltage	Frequency, Motor	Response
1	10	2	990	No response
2	10	2	990	Movements of fingers
3	10	2	990	Movements of wrist and forearm
4	10	2	990	Movements of elbow
5	10	2	990	Movements of shoulder
			Premotor	
6	10	2	990	Mass movements of entire upper extremity, thumb to fingers, passing into generalized convulsions; on several occasions muscles of the neck involved. All these movements were characterized by violence and involved large groups of muscles

CASE 13.—E. R., a girl aged 15, was admitted to the Neurological Institute on May 11, 1938, because of convulsive seizures for ten months. The attacks were characterized by a warning, described as a "prickly feeling," centered in the epigastrium. After this the right arm would flex at the elbow, the right hand flex at the wrist and the right wrist be brought up to the cheek. The patient would then suddenly become unconscious, and if she was standing at the time would fall to the ground. Convulsive movements then became generalized.

Examination.—Neurologic examination revealed slight hypoplasia of the right arm, which may have no significance since the patient was left handed. There were occasional twitching movements of the right hand. Successive movements could not be executed as well with the right hand as with the left. There were slight hyperreflexia on the right and an equivocal Babinski sign on the right. The right hand grip was slightly less strong than the left, but there was no gross weakness otherwise and no disturbance in gait.

Laboratory examination gave results within normal limits. The total protein of the spinal fluid was 23 mg. The serologic reactions were negative.

Roentgenograms of the skull were normal. Encephalograms revealed a slight degree of cerebral atrophy, more on the left than on the right.

Operation.—On May 26, 1938, a left temporoparietal osteoplastic flap, which exposed the superior longitudinal sinus and the superior mesial edge of the hemisphere, was turned up without difficulty under local anesthesia and avertin with amylene hydrate. The cortex was normal in appearance.

Electrical stimulation was carried out, responses were recorded and photographs of the brain were taken at this time, with the various points of stimulation identified by numbers. Unfortunately, however, this is the second of 3 cases (see cases 12 and 14) in which the films were lost.

The operator's notes regarding the stimulations made at the operating table are detailed, and yield considerable information pertinent to the present question, even without the aid of the photographs. In analyzing them, it is noted that the pacchionian granulations along the superior mesial border of the hemisphere were divided, together with the superior anastomosing veins, and electrical stimulation was carried out over the entire exposed cortex up to the mesial surface of the hemisphere. Over eighty cortical excitations were thus made, with the currents used and the responses obtained recorded in detail.

Focal responses were elicited from the upper extremity by stimulating the lateral surface of the hemisphere right up to its superior mesial border. At no point on the free lateral convexity of the hemisphere did stimulation produce focal responses in the upper extremity. At one point only (point Y), situated on the curved edge of the superior mesial border of the hemisphere in close relationship to the pacchionian granulations, did electrical excitation elicit any response in the lower extremity. This response consisted of clonic movements rapidly involving the entire lower extremity, the abdominal musculature on the right and even the right arm. It was entirely different from the fine focal responses obtained from the various parts of the upper extremity, could hardly be considered focal at all, and, indeed, actually resembled minor jacksonian convulsions. Three successive stimulations of this one point produced the same reaction.

Stimulation of the Left Cortex with the Thyratron Esthesiometer (Avertin-Local Anesthesia).—A greatly abbreviated summary of the results of stimulation in this case follows:

Area Stimulated	Frequency	Amperage	Voltage	Response
2	100	22.8	1.08	Swallowing movements
1	100	22.8	1.08	Extension of thumb
F	100	21.5	1.26	Extension of 1st and 2d fingers
G	100	23.0	0.90	Extension of 3d and 4th fingers
J	100	11.0	0.90	Extension of 5th finger
K	100	12.4	0.72	Abduction of 5th finger
I	100	11.7	0.90	Abduction of index finger
O	100	13.0	0.90	Adduction of hand and wrist, and pronation and flexion of forearm
E	100	22.8	1.08	Adduction of arm
N	100	22.8	1.08	Abduction of arm
R	100	22.8	1.08	Contraction of deltoid
U	100	22.8	1.08	Contraction of posterior group of shoulder girdle muscles
Y (superior mesial border)	100	22.8	1.08	Clonus of right leg, spreading to abdomen and thence to tonic convulsion of right hand; lasted about 30 seconds, left arm or leg not involved
Y	100	22.8	0.72	Twitching of right foot, going immediately into convulsion, which spread up leg, thigh and abdomen

CASE 14.—A. K., a woman aged 50, who was admitted to the Neurological Institute on Jan. 27, 1938, had had convulsive attacks every week or ten days for the past twenty-four years. The attacks were preceded by a peculiar aura, consisting of a strange sensation in the stomach, which passed upward through the chest to the head, followed immediately by loss of consciousness and frequently by falling to the ground. Clonic movements involved the right arm only. The attack lasted for a few minutes. Therapy with phenobarbital had been conscientiously tried, without relief.

Examination.—The results were entirely negative, except possibly for slight right hyperreflexia.

Laboratory examinations yielded nothing of importance. The total protein of the spinal fluid was 34 mg. per hundred cubic centimeters. Serologic reactions were negative.

Roentgenograms of the skull were normal. Encephalograms showed mild left cerebral hypoplasia.

Operation.—On March 30, 1938, under cocaine anesthesia, a left cerebral exploration was made. The dura was not under increased tension and was opened widely. The subarachnoid space was thicker than usual, and contained a large amount of fluid. In several areas the subarachnoid space was 4 mm. in thickness. The gyri appeared slightly narrower and more distinct than normal, and the brain was slightly firmer on palpation, but these changes were not localized.

Electrical stimulation was carried out, with the responses recorded for thirty-three vertical excitations. Photographs of the brain were taken at this time, with the various points of stimulation identified by numbers. This is the third of the 3 cases (see cases 12 and 13) in which the films were lost.

Stimulation of Left Cortex with the Thyratron Esthesiometer (Local Anesthesia).—The operator's notes regarding the stimulation made at the operating table are here given in abstract form. It should be noted that the pacchionian granulations along the superior mesial border of the hemisphere were divided, together with the superior anastomosing veins, and electrical stimulation was

carried out up to the mesial surface of the hemisphere. With this in mind, the notes contribute considerable information in their own right, since they reveal the fact that responses in the shoulder were elicited by stimulating the lateral surface of the hemisphere up to its superior mesial border, whereas no responses in the lower extremity were obtained by stimulating the lateral surface of the hemisphere at any point.

Area Stimulated	Amperage	Voltage	Frequency	Response
2	20	3	..	Contraction of masseter muscles; closure of mouth
4	21	2	..	Eyelids opened
5	17	2	..	Flexion of all fingers; adduction of wrist
6	20	2	..	Flexion of elbow
7	20	2	..	Flexion of elbow, with motion of shoulder
8	22	2	..	Movements of muscles about shoulder
9	(points just mesial to 8 on motor gyrus which were revealed after lysis of pachionian granulations)			Slight motion of shoulder
9′	(same point as above, but contacts were a little longer)			Convulsion of right upper extremity

In the 14 cases reported, movements of the upper extremity were obtained by stimulation of the lateral surface of the cerebral hemisphere as far upward as the superior mesial border. In no instance were movements of the lower extremity elicited by stimulation of the lateral surface of the cerebrum. In 1 case movements of the leg were obtained by stimulating the mesial surface of the hemisphere. In 1 instance focal contraction of the rectal sphincter, without other discernible motor reaction, was obtained by stimulation of the mesial surface of the cerebrum in the region of the gyrus cinguli.

COMMENT

It is evident, after a critical review of the literature, that the primary motor centers for the lower extremity have never, in the past, been satisfactorily studied in the human brain. The concept that the primary motor areas for the lower extremity are situated on the lateral surface of the hemisphere would seem to have found its way into the early literature, and even into the standard textbooks of anatomy, on meager, and even questionable, grounds. Indeed, there is considerable evidence that the commonly accepted localizations for the leg centers in the human brain were based almost entirely on observations made on the brains of experimental animals.

The superior mesial border of the cerebral hemisphere in man is a relatively dangerous region to expose, which doubtless explains why it has not been more thoroughly studied. Keen once lost an epileptic patient from uncontrollable hemorrhage which he encountered in attempting to expose this region. Cushing was twice forced to discontinue exposure of this area because of severe bleeding; he stated:

> There is no portion of the hemisphere's surface more difficult to freely expose than its mesial edge near the upper end of the sulcus centralis (Rolandic) . . .

It is unusual to have this inaccessible edge of the hemisphere so freely exposed as to allow of cortical stimulation.

Penfield also said:

The danger of bleeding from sinus or contributory veins makes it unwise to stimulate here unless it is clearly necessary.

Because the superior mesial border of the hemisphere is so difficult to expose and study directly in man, and because it had already been thoroughly established that the primary motor centers for the lower extremity were located on the lateral surface of the hemisphere in animals, the assumption that they were similarly located in man was natural and was freely accepted as true by both clinicians and anatomists.

The 14 cases which I have had the opportunity of studying constitute, however, considerable evidence against the correctness of the old and generally accepted localization of the primary motor centers for the lower extremity on the lateral surface of the hemisphere in man. In fact, the cases here reported indicate that the primary motor centers for the upper extremity commonly extend upward on the lateral surface of the hemisphere as far as the superior mesial border, and that the leg centers, as a rule, are situated entirely on the mesial surface of the hemisphere.

The number of cases reported is admittedly small. On the other hand, it is the only series of similar observations thus far reported. Moreover, importance must attach itself to the fact that the findings were essentially the same in each of the 14 consecutive cases examined. A certain amount of variation in anatomic structure normally occurs everywhere in the body, and undoubtedly cases will be observed in which the findings are at variance with those recorded here. From my own experience, however, I believe that the observations and conclusions here stated regarding the upward extent of the shoulder area and the position of the leg area will, with time, be generally confirmed.

An upward "migration" of the "motor cortex" in man to a position on the lateral surface of the cerebral hemisphere higher than it occupies in any of the other primates is indicated by the observations reported here. This upward shift, which is unique for man, has probably been influenced, in part, by two factors. The first is liberation of the forelimb from the routine burden of locomotion, with its consequent freedom to acquire a great number of new and complicated activity patterns. The second factor is man's acquisition of the faculty of speech and other forms of symbolic expression. The corresponding expansion of the cortical areas serving speech and the forelimb would seem to have crowded the cortical areas for the hindlimb upward and over the superior border of the hemisphere and on to its mesial surface.

SUMMARY

It has long been commonly accepted in the literature and in the standard textbooks of anatomy that the primary cortical centers for the lower extremity in man were situated on the lateral convexity of the cerebral hemisphere. A critical review of the literature, however, indicates that this concept became established on the basis of a wholly inadequate number of observations made on the human brain—in fact, largely on observations made on the brains of experimental animals.

Observations made by me as a result of electrical stimulation along the superior mesial border of the human cerebrum in 14 consecutive cases indicate that the primary motor area for the upper extremity commonly extends upward on the lateral surface of the cerebral hemisphere as far as its superior mesial border, while the leg, as a rule, is represented only on the mesial surface of the cerebrum.

An upward "migration" of the primary motor strip, unique in man, is implied by the observations reported here. It seems probable that this has been influenced by two factors: (1) "liberation" of the upper extremity from the routine burden of locomotion, with its consequent elaboration of new and highly complex functions, and (2) acquisition of speech and other forms of symbolic expression. These new functional acquisitions have been accompanied by corresponding expansion of the cortical areas representing the tongue, mouth, lips and upper extremity, with the result that the cortical representation for the leg has been crowded farther and farther upward on the lateral surface of the hemisphere until it was finally pushed "over the top" onto the mesial surface of the hemisphere.

Focal contractions of the rectal sphincter, produced by stimulation of the mesial surface of the cerebral hemisphere, are here reported for the first time.

RELATION OF INTRACRANIAL TUMORS AND SYMPTOMATIC EPILEPSY

WILDER PENFIELD, M.D.

T. C. ERICKSON, M.D.
AND
I. TARLOV, M.D.
MONTREAL, CANADA

That focal epileptic seizures may be the direct result of the presence of a tumor of the brain has long been recognized (Hughlings Jackson,[1] Bramwell,[2] Biemond,[3] Lehoczky,[4] Walshe,[5] Furlow and Sachs,[6] List,[7] and Pedersen [8]). The incidence of epileptiform seizures in cases of such a tumor and the relative importance of cerebral localization, histologic structure and rate of growth are analyzed in the present communication. Inquiry is made also concerning the continuance of seizures after extirpation of the tumor.

This report is based on a study of 703 cases of intracranial tumors, all of which (except 6 cases of pontile tumors) were verified by histologic study. "Intracranial tumor" is interpreted as meaning an expanding intracranial lesion. This would include neoplasms, tuberculomas, abscesses of the brain and extracerebral and intracerebral hematomas.

From the Montreal Neurological Institute and the Department of Neurology and Neurosurgery, McGill University.

1. Jackson, J. H.: Localized Convulsions from Tumor of the Brain, Brain **5**:364-374, 1882; reprinted in Taylor, J.; Holmes, G., and Walshe, F. M. R.: Selected Writings of John Hughlings Jackson, London, Hodder & Stoughton, Ltd., 1931, p. 341.

2. Bramwell, B.: Intracranial Tumors, Philadelphia, J. B. Lippincott Company, 1888.

3. Biemond, A.: Epilepsie und Hirngeschwulst, Psychiat. en neurol. bl. **36**: 162-168, 1932; abstracted, Zentralbl. f. d. ges. Neurol. u. Psychiat. **65**:540, 1933.

4. Lehoczky, T.: Hirngeschwulst und Epilepsie, Deutsche Ztschr. f. Nervenh. **138**:117-145, 1935.

5. Walshe, F. M. R.: Intracranial Tumors: A Critical Review, Quart. J. Med. **24**:587-640, 1931.

6. Furlow, L. T., and Sachs, E.: The Occurrence of Convulsions in a Series of Over Seven Hundred Verified Intracranial Tumors, South. Surgeon **5**:179-191, 1936.

7. List, C.: Epileptiform Attacks in Cases of Glioma of the Cerebral Hemispheres: Relation to Location and Histologic Type of Glioma, Arch. Neurol. & Psychiat. **35**:323-350 (Feb.) 1936.

8. Pedersen, O.: Ueber epileptische Anfälle beim Tumor cerebri, Zentralbl. f. Neurochir. **3**:204-214, 1938.

To allow a study of postoperative results, no case of more recent date than Sept. 1, 1938 has been included.

Under the heading of epileptiform fits or epileptic seizures we have included sensory, motor and psychic phenomena which may be considered to result from the irritating effect of these lesions. The majority of the seizures were frankly convulsive and usually focal in origin. However, visual, auditory, olfactory and gustatory hallucinations, although rare, as well as spells of loss of memory (2 cases) and of sudden loss of consciousness, are nevertheless to be considered seizures. The form of these attacks does not differ from that of the seizures often seen in so-called idiopathic epilepsy, and nothing is to be gained by reserving the term "epileptic" solely for the latter.

This study is concerned chiefly with tumors above the tentorium.

LOCATION OF LESION

Preliminary analysis must be made according to the localization of the expanding lesion. Of this series of 703 cases of intracranial tumors[9] there were infratentorial expanding lesions in 149, or 21 per cent. In 30 of the 149 cases, or in 20 per cent, there were sudden recurring episodes which might perhaps be called seizures, but were of a peculiar type. The questions of the attacks which are secondary to expanding lesions below the tentorium will form the subject of a separate study. It is sufficient to say that in only 4 of the 149 cases did the patient suffer from ordinary grand mal epilepsy. In 2 cases of this type metastasis from the cerebellar neoplasm to a position above the tentorium was proved. In another extreme hydrocephalus was present, and in a fourth the history suggested essential epilepsy complicated by tumor of the posterior fossa.

In general it may be said that epileptic seizures are not produced by lesions of the cerebellum, and that seizures resulting from tumors of the brain stem below the tentorium are to be considered of a different type.

Tumors of the pituitary region constituted 7 per cent of the total number (49 cases). In only 4 of these was the tumor associated with epilepsy. In 1 case in which attacks occurred autopsy revealed extension of a chromophobic adenoma into the frontal lobe. In the second and third cases craniopharyngeal epitheliomas were situated above the sella. In 1 of these the attacks were characterized by falling without loss of consciousness; in the other, by simple loss of consciousness. In the fourth case, that of a chromophobic adenoma, tonic fits occurred only two days before death. It is evident that intrasellar neoplasms do not produce seizures unless they escape from the sella turcica, but that suprasellar

9. In many of these cases operation was carried out by Dr. William Cone or Dr. Arthur Elvidge, our associates.

tumors may do so when they are large enough to embarrass the basal regions of the brain.

Supratentorial tumors constituted 79 per cent of the total number in this series, seizures occurring in 45 per cent of the cases. If cases of pituitary tumor are excluded, fits occurred in 48 per cent. Intracerebral tumors occurred almost twice as frequently as extracerebral ones, in 326 as against 181 cases. Tumors of the intracerebral group were associated with epileptiform seizures in 51 per cent of the cases, as against 47 per cent for the extracerebral group. This slight difference in incidence may be due to the fact that among the extracerebral lesions subdural and extradural hematomas are included, in cases of which seizures are rare. When we limit our consideration to neoplasms, we obtain an incidence of 51 per cent for epileptiform fits among the cases of intracerebral tumors and of 62 per cent among those of extracerebral neoplasms. When tumors of the basal ganglia and third ventricle are omitted from the intracerebral group, the incidence of fits rises to 55 per cent.

Before attempting to judge the regional susceptibility of different parts of the brain to production of seizures, we decided to determine the mass of the different units of the hemisphere as they are ordinarily denominated. Consequently, a normal cerebral hemisphere which had been fixed in formaldehyde was divided into its various lobes and the volume displacement determined, with the following results: occipital lobe, 50 cc.; temporal lobe, 120 cc.; parietal lobe, 170 cc., and frontal lobe, 175 cc. With the volume of the occipital lobe as 1, the relative volumes of the other regions were: temporal lobe, 2.4; parietal lobe, 3.4, and frontal lobe, 3.5. Of course these divisions were arbitrary, the frontal lobe being considered as all the hemisphere anterior to the central sulcus. The designations of the other divisions are those of the Basle Nomina Anatomica.

These figures serve to emphasize the fact that only relative frequencies of fits associated with different regions can be considered valid for a study of their comparative regional incidence. If the number of tumors in various lobes of the brain is corrected for the relative volume or mass of the respective lobes, the following factors are obtained: parietal lobe, 1; occipital lobe, 1.27; frontal lobe, 1.5, and temporal lobe, 1.77. This indicates that relative to the absolute mass of the various regions tumors are a little more frequent in the temporal than in the parietal lobe. On the other hand, as surgical approach is made by preference through the temporal region, there may be a tendency to call a tumor which lies between the two lobes temporal rather than parietal. In general, the difference of incidence is not marked in the various lobes of the hemisphere.

Seizures occurred in 68 per cent of the cases of tumor of the parietal lobe, which was a slightly greater frequency than that for the temporal and the frontal region (table 1). Tumors involving the frontoparietal

region were associated with fits in 71 per cent of cases, those involving the frontotemporal in 80 per cent and those involving the temporal in

TABLE 1.—*Relation of Epileptiform Fits to Tumors in Various Locations of the Brain in 256 Patients*

Region	Number of Tumors	Percentage with Fits
Frontal	115	53
Parietal	74	68
Temporal	94	48
Occipital	28	32
Frontoparietal	21	71
Parieto-occipital	15	47
Parietotemporal	12	67
Temporo-occipital	3	67
Frontotemporal	5	80
Parietotemporo-occipital	10	40
Frontoparietotemporal	1	..
Frontoparieto-occipital	3	33
Hemisphere	91	27
Third ventricle	20	32
Thalamus and basal ganglia	12	8
Pituitary region	49	8
Infratentorial	149	3
Lateral ventricle	1	..
Total number in all regions	703	37

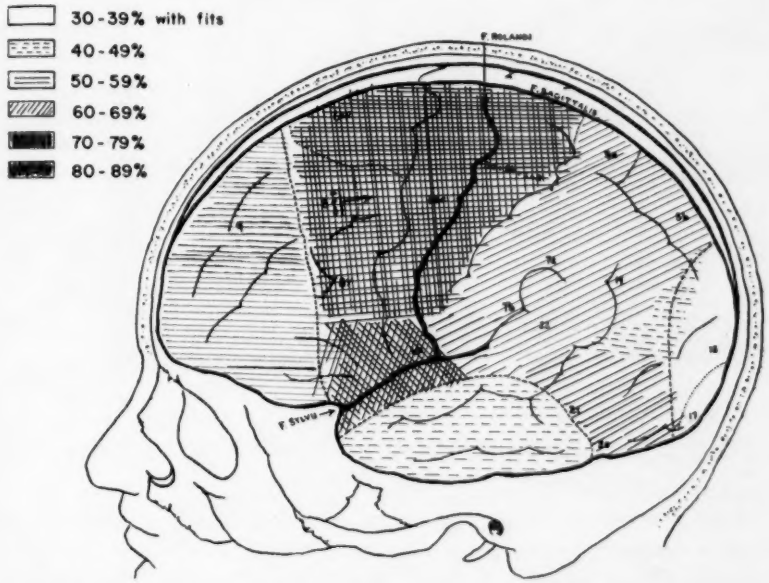


Fig. 1.—In this diagram the incidence of fits with tumors of various portions of the cerebral hemispheres is graphically illustrated. It is evident that the incidence is greatest with tumors in proximity to the central sulcus.

48 per cent. The lowest incidence of seizures occurred with the tumors of the occipital lobe—32 per cent, or 28 cases. It is apparent that the incidence increases as the site of the tumor approaches the rolandic fissure (fig. 1).

This agrees in general with the results of Gibbs,[10] who found seizures most frequent with tumors in the parietal lobe. Allen [11] reported some type of epileptiform attack in 52.5 per cent of 40 cases of tumors involving the occipital lobe. In only 10 per cent were the attacks preceded by visual aura, and the incidence for tumors confined to the occipital lobe was 30

TABLE 2.—*Regional Distribution of the More Common Types of Cerebral Gliomas in Relation to the Occurrence of Epileptiform Fits* *

			Frontal	Parietal	Temporal	Occipital		Other Regions
Astrocytoma.....	64	With fits.... 45	11	9	15	1	9	3 temporoparietal 2 frontotemporal 1 frontoparietal 2 third ventricle 1 hemisphere
		Without fits 19	7	2	3	0	7	3 third ventricle 2 basal ganglia 1 thalamus 1 hemisphere
Glioblastoma Multiforme	103	With fits.... 38	4	9	9	2	14	4 hemisphere 1 frontoparietal 4 parieto-occipital 1 frontotemporal 4 parietotemporal
		Without fits 65	14	8	13	9	21	8 hemisphere 1 thalamus 3 basal ganglia 3 frontoparietal 5 parieto-occipital 1 frontotemporal
Oligodendroglioma	13	With fits.... 12	9	1	1	..	1	parieto-occipito-temporal
		Without fits 1	1	..	..	..	..	.....
Astroblastoma....	17	With fits.... 10	6	1	1	..	2	1 temporoparietal 1 frontoparietal
		Without fits 7	1	1	1	1	3	1 hemisphere 1 third vetricle
Ependymoma.....	9	With fits.... 3	1	1	..	..	1	parietofrontal
		Without fits 6	1	..	..	..	5	4 third ventricle 1 parieto-occipito-temporal

* The incidence of fits in the astrocytoma and glioblastoma multiforme groups in the various regions is particularly worthy of comparison.

per cent. Frazier and Waggoner [12] recorded convulsions in 25 per cent of their 40 cases of occipital tumor.

10. Gibbs, F. A.: Frequency with Which Tumors in Various Parts of the Brain Produce Certain Symptoms, Arch. Neurol. & Psychiat. **28**:969-989 (Nov.) 1932.

11. Allen, I. M.: A Clinical Study of Tumors Involving the Occipital Lobe, Brain **53**:194-243, 1930.

12. Frazier, C. H., and Waggoner, R. W.: Tumors of the Occipital Lobe: A Review of Forty Cases, Arch. Neurol. & Psychiat. **22**:1096-1097 (Nov.) 1929.

In the whole series there were 20 cases of tumor of the third ventricle, and in 7 of these seizures occurred. In some instances the attacks showed characteristics of autonomic epilepsy (Penfield [13]). In others the pattern was that of the tonic or decerebrate fit. In still others the pattern betrayed the fact that the tumor extended outward into the hemispheres. It is noteworthy that unconsciousness came early in these cases, but

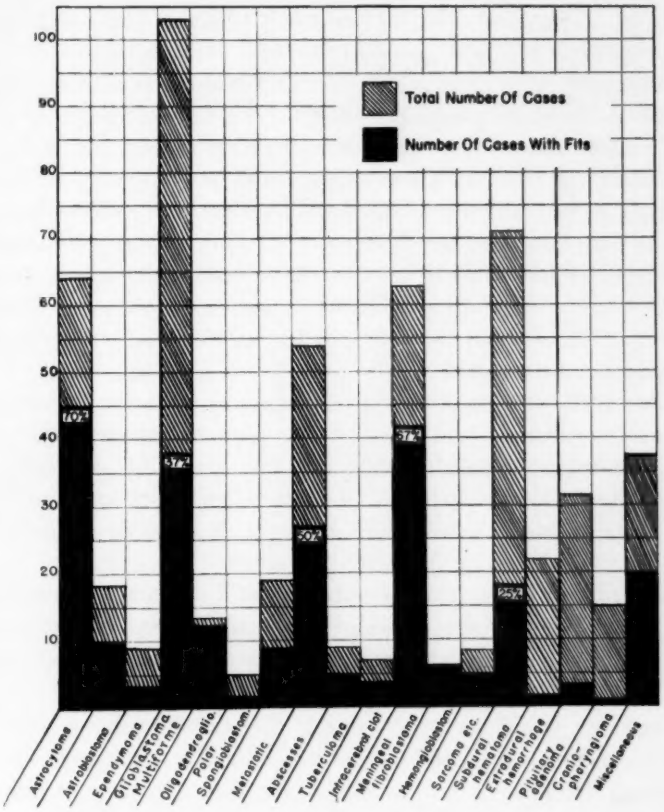


Fig. 2.—This diagram shows the total number of cases in which epileptiform fits occurred for each of the histologic types of tumors in our series. The percentage in which fits occurred is indicated for each of the groups in which it is sufficiently large to be significant. Under the heading of *Miscellaneous* are included unclassified gliomas, neuroepitheliomas, pinealomas, ganglioneuromas, arteriovenous aneurysms, angiomas, cholesteatomas, dermoid cysts and colloid cysts. Under *Sarcoma, etc.*, are included 5 sarcomas, only 1 of which was associated with seizures, and 4 less malignant tumors, 3 of which were associated with seizures.

13. Penfield, W.: Diencephalic Autonomic Epilepsy, A. Research Nerv. & Ment. Dis., Proc. **9**:645-663, 1930.

this, together with the seizures secondary to neoplasms of the posterior fossa, will be discussed in further detail in a separate report.

NATURE OF LESION

A. Gliomas.—There were 230 cases of histologically verified gliomas in this series (table 2 shows the distribution of the more common types only). Of the 103 cases of glioblastoma multiforme, seizures occurred in only 38, or 37 per cent (fig. 2), and of 64 cases of astrocytoma this complication appeared in 45, or 70 per cent. Thus the relatively benign astrocytoma was associated with epileptiform seizures almost twice as frequently as the more malignant glioblastoma. Selection of the focal [14] seizures only in each group makes the contrast more striking, as such seizures occurred about two and a half times as frequently in cases of astrocytoma as in those of glioblastoma. This striking difference in incidence is not explained by the difference in habitual anatomic location of the two types of tumor, as is indicated in table 2. Whether or not it is due to differences in microscopic structure is not at once evident because of the great difference in rate of growth, and consequently in duration of the presence of the tumor.

On the other hand, the astrocytomas may be divided into three types (Elvidge, Penfield and Cone [15]). The rate of growth of the three types is similar, but astrocytoma diffusum infiltrates without destroying the ganglion cells, while the gemistocytic and piloid types are much more discrete. The incidence of seizures, however, is about the same for all three types, as is shown by the following figures.

In the group of astrocytomas occurring in a supratentorial situation, seizures occurred in 11 of 15 cases of astrocytoma diffusum, in 17 of 21 cases of gemistocytic astrocytoma and in 12 of 13 cases of piloid astrocytomas. There is, then, no marked difference in the incidence of fits in these subgroups, which strongly suggests that the duration of the tumor is more important than its histologic relationship to adjacent nerve cells.

Between glioblastoma and astrocytoma there are certain constant histologic differences. Glioblastoma is a little more likely to extend through the white matter and basal ganglia; astrocytoma is more apt to be cortical, as well as subcortical. Astrocytoma, as already pointed out, may either infiltrate without destroying or expand and compress by cyst formation with little or no infiltration. Glioblastoma shows conspicuous formation of new vessels and rapid closure of vessels resulting in focal ischemic softening, scattered small cysts and a variety of neurog-

14. By "focal" seizure is meant one which begins with an isolated cortical phenomenon. In a strict sense nearly all seizures are no doubt focal.

15. Elvidge, A.; Penfield, W., and Cone, W.: The Gliomas of the Central Nervous System, A. Research Nerv. & Ment. Dis., Proc. **16**:107-181, 1937.

lial reactions, which may be seen in the brain itself before the obvious arrival of neoplastic cells. It may well be that these histologic differences have some relation to the difference in incidence of seizures, but fair comparison is impossible. The glioblastoma multiforme may run its course and end in the patient's death in from three to six months, whereas the astrocytoma may be present for three years before it attracts attention to itself. It seems likely that if patients with glioblastoma survived a year or two longer more of them would have seizures.

From a statistical standpoint, gliomas, other than glioblastomas and astrocytomas (fig. 2), were so few in our series that the figures for the incidence of epilepsy cannot be stressed. It is of interest, however, that in 12 (92 per cent) of 13 cases of oligodendroglioma the tumor was associated with epilepsy, which was focal in all instances. The clinical course in these cases was often long, indicating slow growth of the tumor; moreover, the tumors were apt to be superficial in origin. In the only case in which oligodendroglioma was not associated with epilepsy growth was unusually rapid, and mitotic figures were numerous. Of the 17 cases of astroblastoma, there were seizures in 10 (59 per cent).

B. Meningeal Tumors.—Of the 71 meningeal tumors of various sorts 48 (68 per cent) were associated with seizures. Of the 63 meningeal fibroblastomas, 42 (67 per cent) were associated with seizures. This is almost exactly the same incidence of seizures as was found with the astrocytomas. The meningeal tumors are extracerebral and completely encapsulated. The only factor which the two groups have in common is their relatively slow growth and consequent long-continued alteration of the adjoining cerebral tissue. There is no difference in the types of seizure produced by the two types of tumor, aside from that dependent on their most characteristic locations. Malignant meningeal tumors—sarcomas and fibrosarcomas—occurred in only 5 cases. In only 1 of these were there epileptiform fits.

C. Subdural Hematomas.—There were 71 cases of subdural hematoma occurring above the tentorium. Of these, seizures were observed in only 18 (25 per cent), and in only 4 cases were seizures the initial symptom. When cases in which fits occur are studied in detail, some evidence of intracerebral lesion is commonly present. As, happily, the patient does not die and so opportunity for autopsy does not arise, complete report is impossible, but the evidence suggests that if the cases of cerebral contusion were eliminated the number of instances of subdural hematoma associated with seizures would fall much lower, and perhaps reach the vanishing point. Kunkel and Dandy [16] reported convulsions in 12 per cent of their 48 cases of subdural hematoma, which is even lower than our figures.

16. Kunkel, P. A., and Dandy, W. E.: Subdural Hematoma, Arch. Surg. **38**:24-54 (Jan.) 1939.

D. Abscess of the Brain.—There were 54 cases of intracerebral abscess in this series. Convulsive seizures occurred in 27 (50 per cent) of the cases. Although the seizures were not commonly an initial symptom, they usually occurred early. Typically, there were only one to four seizures in all, and then no more attacks, even though the abscess had a duration of several months before operation. We must conclude that in a certain phase of acute development of the abscess fits are particularly likely to occur, but that with the further evolution of the abscess this phase is soon passed. These seizures, of course, are to be distinguished from the late seizures which may follow successful drainage of an abscess. This will be discussed later.

FREQUENCY OF EPILEPTIC SEIZURES AS INITIAL SYMPTOM

When epileptiform seizures occur as the first or only symptom of tumor of the brain, their true significance is often missed. Furthermore,

TABLE 3.—*Incidence of Epileptiform Fits as an Initial Symptom**

	Astrocytoma	Meningeal Fibroblastoma	Glioblastoma Multiforme	Subdural Hematoma
Total number of cases	64	63	103	71
Total number in which fits occurred	45	42	38	18
Percentage in which fits occurred	70	67	37	25
Number in which fits were initial symptom	27	26	14	4
Percentage of total incidence in which fits were initial symptom	60	62	37	22

* The incidence of fits as an initial symptom is closely paralleled by the total incidence of fits in each of the four groups of tumors.

the difference in the relative times of onset of fits associated with various types of tumor is helpful in differential diagnosis. Seizures constituted the initial symptom in 60 per cent of the cases of astrocytoma and in only 37 per cent of the cases of glioblastoma, as may be seen in table 3.

Fits as an initial symptom occurred in 75 per cent of cases of oligodendroglioma and in 62 per cent of cases of meningeal fibroblastoma. In 1 case of an unclassified glioma the patient had seizures for fifteen years before operation, and no other symptom occurred until two years before operation. Many similar instances could be cited from our material. In the case of cerebral abscesses, epileptiform seizures are rarely the initial symptom, but they frequently occur soon after the symptoms which indicate the presence of infection in the mastoids or sinuses. In 17 of 27 cases of abscess with seizures, the attacks began within one month of the onset of trouble of any sort. As has already been pointed out, the incidence of seizures in cases of subdural hematoma is low. However, of the 18 patients with such a lesion who had seizures only 4, i. e., 22 per cent, complained of it as an initial symptom.

In general, 40 per cent of all patients who had seizures complained of them as an initial symptom. This corresponds closely with the findings of Sargent [17] and of Parker,[18] who reported that the seizures were initial in 38 of 67 cases of epilepsy. In analyzing our own results, it becomes apparent that the tumor types which have the highest incidence of seizures also are associated with seizures as a first symptom more frequently than other types. In other words, astrocytomas and meningeal fibroblastomas, which are most frequently associated with fits, have seizures as an initial symptom both relatively and absolutely much more frequently than the glioblastomas and subdural hematomas (table 3). This difference suggests that rapid evolution of a tumor produces other symptoms before fits have time to develop.

EFFECT OF REMOVAL OF LESION

Meningeal Fibroblastoma.—Fifty of the 63 patients operated on for meningeal fibroblastoma have been followed up to the present. The relation between seizures occurring preoperatively and those occurring postoperatively was as follows: Forty-two of the 63 patients suffered from seizures before operation. Of these 42 patients, we were able to follow 29, and of these 19 continued to have fits, while 10 were free from them. It seems probable that patients who are completely cured are much more difficult to trace than those who continue to have trouble.

Twelve of the 21 patients without seizures before operation continued to be free from them after operation, while 9 of them had seizures for the first time after operation. Postoperative seizures usually occurred within six months after operation, but occasionally their onset was delayed for twelve to eighteen months. One patient (W. P.) had no seizures before operation but has had three since, the first being three years after operation. The mere statement that fits occurred postoperatively, however, may suggest something less favorable than the true condition, for we have placed a patient in the group "with fits" even if he had only one slight seizure after the immediate postoperative period.

For example, a woman who had no seizures before removal of a tumor from the left middle fossa had been observed to have jerking of the right arm during sleep since operation. Administration of a small dose of phenobarbital stopped these attacks, but she was nevertheless placed in the group of patients with postoperative seizures. In another case a meningeal tumor was removed from the body of the right ventricle. To make the removal possible, a block of brain was excised posterior to the motor area. Seizures began one month after operation and occurred about every two weeks in the subsequent forty-one months. The attacks were focal in character, obviously arising from a scar at the margin

17. Sargent, P.: Some Observations on Epilepsy, Brain **44**:312-328, 1921.

18. Parker, H. L.: Epileptiform Convulsions: Incidence of Attacks in Cases of Intracranial Tumor, Arch. Neurol. & Psychiat. **23**:1032-1041 (May) 1930.

of the cortical excision or from an adjacent area of cortical injury, and not from the tumor bed.

In a third case in which no attacks were reported before operation, the first focal seizure occurred seven months after operation, the focus being in the region of removal of the tumor. In several instances there has been a history of injury before operation, which might account for the development of fits later on the basis of a cerebral cicatrix alone. That trauma may play a part in the origin of the meningeal tumors is recognized (Penfield [19]). One of our patients had a severe blow on the head three months after operation. His first attack occurred immediately and attacks have recurred habitually since.

Groff [20] reported 24 of 66 cases in which operation was performed for meningeal fibroblastoma and there was complete relief from attacks over an average period of observation of four years. In 4 of the remaining 42 cases in Groff's series in which seizures continued there was recurrence of tumor, but in the others, so far as could be determined, there was no recurrence. Groff recorded 13 cases of postoperative epilepsy in a series of 201 cases in which no convulsive seizures occurred before operation. In 5 of the 13 cases there was recurrence of the tumor. Cushing and Eisenhardt [21] also mentioned the occurrence of fits after the removal of meningiomas when none had occurred before.

Gliomas.—Forty-five of the 64 patients with astrocytoma had seizures before operation. In the former group 27 patients were successfully traced, and 23 of them continued to have fits, while only 4 were relieved. In the group of 19 patients without fits before operation, only 6 were successfully traced; 3 of them had seizures for the first time after operation, and 3 continued to be free from such attacks. These are all patients who have lived more than twelve months after operation. There is definitely a greater tendency for the fits to persist in spite of removal of part or all of the tumor in the case of gliomas than in that of the meningeal fibroblastomas. The reason for the relatively greater number of postoperative seizures is undoubtedly the greater tendency to recurrence on the part of gliomas. However, a patient with a recurrence was free from seizures for one year before death, while another patient with partial removal of an astrocytoma diffusum ceased to have fits after operation.

Of 3 of the patients who had seizures and from whom astrocytomas were removed there was no evidence of recurrence of the tumor, 2 being

19. Penfield, W.: Principles of the Pathology of Neurosurgery, in Nelson Loose-Leaf Living Surgery, New York, Thomas Nelson & Sons, 1932, vol. 2, chap. 6, pp. 303-347V.

20. Groff, R.: The Meningioma as a Cause of Epilepsy, Ann. Surg. **101**:167-175, 1935.

21. Cushing, H., and Eisenhardt, L.: Meningiomas: Their Classification, Regional Behaviour, Life History and Surgical End-Results, Springfield, Ill., Charles C. Thomas, Publisher, 1938.

well after thirty-five and sixty months, respectively. The removal was thought to be complete in both cases. Another patient, from whom a gemistocytic astrocytoma in the right frontal region was completely removed, was free from fits for five and a half years, but then began to have frequent daily focal attacks in the left hand. Recurrence was suspected but could not be proved even after thorough examination. Five months later, however, recurrence of the tumor was verified histologically.

COMMENT

Incidence.—The incidence of epileptic seizures in the present series (45 per cent for supratentorial tumors, or 37 per cent for all intracranial tumors) is a little greater than that reported in other series. Parker [18] found focal seizures in 21.6 per cent of cases; Dowman and Smith,[22] some type of epileptiform seizures in 39 per cent and focal attacks in 21 per cent. Sargent [17] noted seizures in 30 per cent of cases of tumors exclusive of the pituitary and cerebellar types; Furlow and Sachs,[6] in 34 per cent of cases of cerebral tumors, and Pedersen,[8] in 29 per cent of 586 cases anatomically confirmed tumors. Parker arbitrarily excluded cases of jacksonian convulsions without loss of consciousness, a fact which accounts, to a certain extent, for his lower incidence. The incidence (67 per cent) for epileptiform seizures associated with the cerebral meningeal tumors of this series is approximately twice that reported by Groff.[20]

It is possible that the greater incidence of epilepsy in this series is due partly to the interest in epilepsy in this clinic, which brings a greater number of epileptic patients here. On the other hand, because of this interest, careful inquiry has been made at the time of admission and all severe episodes have been discovered, which might otherwise have been overlooked.

We have included subdural hematoma with the neoplasms, and the incidence of seizures (25 per cent) associated with such hematomas is less than that (37 per cent) associated with the tumor group with the lowest incidence, glioblastoma multiforme. Time, i. e., short preoperative history, is the only factor that these two processes usually have in common and that distinguishes them from the groups of tumors with a higher incidence of fits and longer preoperative history—astrocytomas (70 per cent) and meningeal fibroblastomas (67 per cent).

It has already been pointed out that in most of the cases of subdural hematoma associated with seizures there is also present focal cortical laceration or contusion. It is probable, therefore, that simple, uncompli-

22. Dowman, C. E., and Smith, W. A.: Intracranial Tumors: A Review of One Hundred Verified Cases, Arch. Neurol. & Psychiat. **20**:1312-1329 (Dec.) 1928.

cated hematoma which produces increased intracranial pressure but no focal cerebral destruction rarely causes epilepsy. The same is true of internal hydrocephalus. Steadily increased pressure may produce diffuse cerebral destruction, but epileptiform seizures are a rare complication.

We conclude that chronic increase of intracranial pressure, due either to expanding ventricles or to subdural hematoma, only rarely seems to serve as the sole cause of habitual seizures. On the other hand, it is a common experience among neurosurgeons that during direct injection of air into the ventricles an immediate seizure may be produced if the pressure is suddenly raised too high. In spite of this and the experimental evidence that acute increase of pressure increases the tendency to seizures (Elsberg and Pike [23]), our conclusion is that chronic increased intracranial pressure does not produce seizures or increase the tendency to seizures in a case of focal lesion of the hemispheres.

Focal Expanding Lesions.—These seem to compromise the cerebral tissue in a different way. The highest incidence of seizures associated with supratentorial lesions was found in cases of meningeal fibroblastoma, 67 per cent, of astrocytoma, 70 per cent, and of oligodendroglioma, 92 per cent. It was in cases of these tumors, also, that seizures most often formed the initial symptom (62, 60 and 75 per cent, respectively), whereas the fits were initial in only 37 per cent of cases of the rapidly growing glioblastoma group in which there were seizures.

Predisposition.—The question of family and individual predisposition to epileptic seizures should be mentioned at this point. Lennox, Gibbs and Gibbs [24] have described the frequency of cerebral dysrhythmia as shown electroencephalographically in one or both parents of epileptic persons, as well as the almost inevitable presence of dysrhythmia in the patient. Nevertheless, the high incidence of seizures associated with certain tumor types which we have described would seem to minimize the importance of predisposition as a prerequisite to seizures in a case of cerebral tumor. Other elements must be considered as well.

It would seem that the early appearance of increased intracranial pressure in cases of the rapidly growing glioblastoma group calls attention to the condition before seizures have time to develop. With the slowly growing tumors seizures usually appear before the general intracranial pressure is raised.

Tumor Encroachment.—We have already pointed out that we are not able to relate the incidence of fits to the manner of encroachment

23. Elsberg, C. A., and Pike, F. H.: Studies on Epilepsy: Influence of General Increase or Diminution of Intracranial Pressure upon Susceptibility of Animals to Convulsive Seizures, Am. J. Physiol. **76**:593-597, 1926.

24. Lennox, W. G.; Gibbs, E. L., and Gibbs, F. A.: The Inheritance of Epilepsy as Revealed by the Electroencephalograph, J. A. M. A. **113**:1002-1003 (Sept. 9) 1939.

of the tumor, as the different types of infiltrating astrocytoma have a similar incidence of seizures. This incidence is similar also to that for meningeal fibroblastomas, which do not infiltrate at all, but are encapsulated.

Position of Tumor.—There is, however, a definite difference in the incidence of seizures based on the position of the tumor. The nearer the lesion is to the rolandic zone, especially its lower end, the higher the incidence (fig. 1), while tumors of the occipital pole have the lowest incidence of all. The preponderance of glioblastomas over astrocytomas in the occipital lobe may account to some extent for the low incidence of seizures associated with tumors in that region.

We find no evidence that deep neoplasms have a higher incidence of seizures than superficial ones, as has been stated by some authors. The reverse seems to be the case. The zone of highest incidence near the rolandic fissure is that in which electrical stimulation most easily produces seizures in man. It is the only zone of the animal cortex in which "physiologic" fits can be produced by stimulation. It is the zone toward which epileptic "discharge" usually moves in man, whatever may have been the position of the initial focus on the cortex. This would seem to be the area of the cortex most susceptible to the condition which produces epileptic seizures.

Chronicity.—Nevertheless, wherever a lesion may be, the likelihood of its causing epilepsy is influenced by other factors, most important of which seems to be chronicity. Time is required for the establishment of habitual seizures. When the statement is made that glioblastoma produces seizures in only 37 per cent of cases and astrocytoma in 70 per cent, the difference in duration of life with the two tumors must be recalled. Glioblastoma is apt to produce death in from six weeks to six months from onset, while the patient suffering from astrocytoma may live many years. The incidence of fits among patients with glioblastoma at three months is much higher than that among patients with astrocytoma at the same period. This may be due to the rapid alteration in the blood supply of the adjacent part of the brain, which results from the changes in the blood vessels so common with glioblastoma. If patients with glioblastoma could live five years it is conceivable that they would all be epileptic.

Abscess of the Brain.—The incidence of seizures in cases of abscess of the brain is comparatively high at an early and again at a late period in its evolution. It has been pointed out that the early attacks are as a rule few and tend to disappear shortly. It would seem that the rapid advance of the abscess produces a state which disappears as the lesion becomes chronic and encapsulated, only to reappear perhaps years later, after the abscess is replaced by a healed scar.

What happens during the lapse of time in these areas of focal hemispheral injury? The answer can be no more than surmise. There is, in all cases, slowly progressive local degeneration of gray matter. This destruction is produced by progressive local ischemia. Slowly advancing local ischemia would seem to be a more likely cause of seizures than sudden widespread complete anemia. This is to restate the assumption of Hughlings Jackson [25] that an area of partial destruction is more apt to cause seizures than an area of complete destruction.

Extirpation of the Tumor.—The effect on epilepsy of surgical extirpation has been discussed. Even in the group of cases of meningeal fibroblastomas, in which removal was usually complete, the cure of the tendency to attacks was far from invariable. Of 29 patients who had preoperative seizures and who were followed, only 10 became free from attacks. On the other hand, of the 21 patients with meningeal fibroblastoma who did not have preoperative attacks, 12 continued to be free from them and 9 experienced seizures for the first time after operation. Thus, 42 per cent of all patients with meningeal fibroblastoma who could be followed were free from attacks after operation, and 35 per cent of the patients who had preoperative attacks became free. Postoperative seizures in such cases may be easily controlled by medication, but the record of complete cure of seizures by removal of meningeal fibroblastoma differs little from the record of cure by removal of cerebral and meningocerebral cicatrix (41 and 46 per cent, respectively [Penfield [26]]). The results of removal of astrocytoma, as far as continuance of seizures is concerned, is less encouraging, for only 21 per cent of the patients were relieved from seizures.

What is the reason for continuance of seizures after removal of the tumor? One obvious cause, especially in the case of gliomas, is recurrence. Another is operative trauma of the brain incident to removal, which may produce a meningocerebral cicatrix, in which case attacks would be expected only months or years after operation. The most frequent cause seems to be the cortical injury which the neoplasm almost invariably produces in its growth. Even an encapsulated meningeal fibroblastoma, removed with meticulous care, usually leaves behind it, in the area of maximum impingement on the brain, injury or absence of the pia mater. This results in scar and continuing abnormality of cortical circulation. In most such cases it has been our custom to remove any areas of completely softened superficial cerebral tissue after the tumor

25. Jackson, J. H.: A Study of Convulsions, Tr. St. Andrews Med. Grad. Ac. **3**:1-45, 1870; reprinted in Taylor, J.; Holmes, G., and Walshe, F. M. R.: Selected Writings of John Hughlings Jackson, London, Hodder & Stoughton, Ltd., 1931, p. 8.

26. Penfield, W.: Epilepsy and Surgical Therapy, Arch. Neurol. & Psychiat. **36**:449-484 (Sept.) 1936.

was excised. In the present analysis it is not possible to determine whether this procedure has influenced the incidence of postoperative seizures.

At times there seems to be a postoperative condition that produces epilepsy only for a transient period after operation. One patient had his first seizure six weeks after operation and his third and last seizure twelve months after operation, since which he has been free from attacks for fifty-six months, up to the time of writing. In cases in which seizures continued after operation it was found on investigation that the preoperative seizure had in general been more severe and of longer standing than in cases in which the attacks stopped. This was not an invariable rule, but it suggests the possible importance of brain habit (Gowers [27]), personal predisposition or the degree of cortical damage.

The onset of epilepsy only years after injury to the head is well known. By the same token, it might be expected that cerebral scar following operative manipulation would in some cases not make itself felt until years after operation. In such a case recurrence of the tumor would always be suspected by the surgeon. This difficulty of deciding on the cause is illustrated by a case in which there was freedom from fits for five and a half years after removal of an astrocytoma. At this time the patient began to have seizures arising from the brain adjoining the site of removal of the tumor. Study revealed no evidence of recurrence of the tumor but four months later surgical exploration showed recurrence of the tumor, a gemistocytic astrocytoma.

CONCLUSIONS

The slowly growing neoplasms have a higher incidence of secondary epilepsy than the rapidly growing tumors, probably because death terminates the history sooner in cases of the latter type. Seizures form a first symptom also more frequently in cases of the slowly growing tumors. Infiltrating and encapsulated tumors, if they are equally slow growing, have an approximately equal incidence of seizures. Operative removal gives complete relief from seizures twice as often in cases of encapsulated tumors as it does in cases of infiltrating tumors. In our clinic the percentage of "cure" of seizures by operative removal of encapsulated tumors is about the same as that from excision of focal cerebral scars for the relief of epilepsy.

Abscesses of the brain are apt to produce seizures at an early stage and again after the formation of a healed scar. Subdural hematomas have a relatively low incidence of seizures, and the attacks even then seem to be due to cerebral injury that may have resulted from trauma rather than to the hematoma itself.

---

27. Gowers, W. R.: Diseases of the Nervous System, London, Churchill, 1888, vol. 2.

RELATION OF EXPERIMENTAL HISTAMINE HEADACHE TO MIGRAINE AND NON-MIGRAINE HEADACHE

THEODORE J. C. von STORCH, M.D.
BOSTON

Evidence has recently been presented which suggests that the mechanism of migraine headache is similar to that of the so-called histamine headache, first described by Pickering.[1] It is the purpose of this study to investigate other aspects of the relation.

Headache following sudden intravenous injection of small amounts of histamine phosphate is considered to be due to the resultant hypotonicity of branches of the internal and external carotid arteries.[2] Apparently the increased amplitude of the arterial pulsations resulting from the relaxed vessel walls stimulates the periarterial nerve plexus.[2a] Such stimulation when transmitted centrally by the trigeminal nerve and along other as yet undetermined pathways is interpreted as pain.[2b]

Other observations have revealed that migraine headache is accompanied by a similar increase in the amplitude of cranial arterial pulsations, limited, however, to branches of the external carotid artery.[3] It has been demonstrated that the amplitude of these pulsations is decreased by the vasoconstrictor action of ergotamine tartrate, the decrease corresponding with relief of the headache.[3] Ergotamine tartrate

---

Aided by a grant from the Rockefeller Foundation.

From the Neurological Unit of the Boston City Hospital and the Department of Neurology of the Harvard Medical School.

Assistant Professor of Neurology, Boston University School of Medicine; Instructor in Neurology, Harvard Medical School.

1. Pickering, G. W.: Observations on the Mechanism of Headache Produced by Histamine, Clin. Sc. **1**:77, 1933. This type of histamine headache is not to be confused with histamine "erythromelalgia of the head," recently described by Horton, MacLean and Craig (Horton, B. T.; MacLean, A. R., and Craig, W. M.: A New Syndrome of Vascular Headache, Proc. Staff Meet., Mayo Clin. **14**: 257, 1939).

2. (*a*) Clark, D.; Hough, H., and Wolff, H. G.: Experimental Studies on Headache: Observations on Histamine Headache, Arch. Neurol. & Psychiat. **35**: 1054 (May) 1936. (*b*) Northfield, D. W. C.: Some Observations on Headache, Brain **61**:133, 1938.

3. Graham, J. R., and Wolff, H. G.: Mechanism of Migraine Headache and Action of Ergotamine Tartrate, Arch. Neurol. & Psychiat. **39**:737 (April) 1938.

acts as a vasoconstrictor on branches of the external but not of the internal carotid artery.[4] It therefore has little effect on histamine headache.

In both histamine headache and migraine headache vasodilatation is probably the ultimate cause of the pain. In histamine headache the vasodilatation is sudden, transitory and generalized in all branches of both the internal and the external carotid artery. In migraine headache the vasodilatation is recurrent, prolonged, more gradual in onset, often localized and primarily in the branches of the external carotid artery.[5]

Such similarity renders it not unreasonable to ask whether patients subject to migraine are overly susceptible to histamine. Is it easier to produce histamine headache in patients subject to migraine headache? Are the resultant headaches similar to migraine attacks? How do these observations compare with the effect of histamine in subjects suffering from other chronic recurrent headache and in those not subject to headache of any type. In an attempt to answer these questions, histamine headache was induced in these three types of persons.

METHOD

According to Weiss and his associates,[6] as much as 500 mg. of histamine phosphate may be orally administered to human subjects without causing objective or subjective changes. Subcutaneous injections of from 0.5 to 1 mg. are followed by variable responses, one of which may be headache. Intravenous infusion of histamine does not cause headache during the period of infusion. In an adult of average weight, the sudden intravenous injection of from 0.01 to 0.03 mg. of histamine phosphate consistently causes a metallic taste, a facial flush, increase in pulse rate and a sensation of tension within the head. An increase to 0.07 mg. per injection occasionally results in headache, while injection of 0.1 mg. invariably produces headache. It was found by trial that injection of 0.05 mg. rarely caused a headache in subjects of average weight who were not subject to headache, while at the same time it invariably caused the vascular changes already noted. This was termed the "active subthreshold dose" with respect to headache. This amount being considered the active subthreshold dose for subjects weighing between 145 and 175 pounds (65 and 79 Kg.), a tabulation of subthreshold doses of a 1:10,000 solution

4. Pool, J. L., and Nason, G. I.: The Comparative Effect of Ergotamine Tartrate on the Arteries of the Pia, Dura and Skin of Cats, Arch. Neurol. & Psychiat. **33**:276 (Feb.) 1935.

5. It is not unlikely that transitory localized areas of vasodilatation, and even vasoconstriction, occur in branches of the internal carotid artery during certain phases of a migraine attack. Thus may be produced the scotomas, aphasia, paresthesia and other associated phenomena of central origin.

6. Weiss, S.; Robb, G. P., and Ellis, L. B.: The Systemic Effects of Histamine in Man with Special Reference to the Responses of the Cardiovascular System, Arch. Int. Med. **49**:360 (March) 1932.

of histamine phosphate was compiled, approximating 0.00034 mg. of histamine per pound (0.00755 mg. per kilogram) of body weight.

Weight of Subject	Dose
85 to 115 pounds (39 to 52 Kg.)	0.03 mg. (0.3 cc.)
115 to 145 pounds (52 to 66 Kg.)	0.04 mg. (0.4 cc.)
145 to 175 pounds (66 to 79 Kg.)	0.05 mg. (0.5 cc.)
175 to 195 pounds (79 to 89 Kg.)	0.06 mg. (0.6 cc.)
195 to 225 pounds (89 to 102 Kg.)	0.07 mg. (0.7 cc.)
225 to 250 pounds (102 to 113 Kg.)	0.08 mg. (0.8 cc.)

For intravenous injection, 1 cc. of a standard 1:1,000 solution of histamine phosphate was diluted with 9 cc. of sterile physiologic solution of sodium chloride. Each cubic centimeter of this solution contained 0.1 mg. of histamine phosphate (0.03 mg. of histamine base). Thus, for example, the sudden intravenous injection of 0.5 cc. of this solution introduced 0.05 mg. of histamine phosphate into the blood stream. All injections were made into the antecubital veins. The patient sat or reclined during the injection. Posture apparently had no effect on the results. In order to avoid untoward reactions, patients were not used who were subject to infections of the upper respiratory tract, bronchitis, asthma, cardiac asthma, myocardial failure and coronary disease.

Injections were given to patients without mention of subsequent headache. They were told that soon after the injection they would "feel queer." Instructions were given to report and describe at once any sensations which they experienced. After all reactions had disappeared, the patient's brief report was amplified by specific questioning. Reactions were timed as to onset and duration. They occurred in the following sequence: metallic taste (not invariably reported), objective and subjective facial flush, subjective intracranial "fulness" and intracranial throbbing. The metallic taste was reported in from ten to twenty-five seconds and was followed by the other symptoms at approximately five second intervals. When a headache occurred, it usually did so within twenty to sixty seconds after injection. All headaches were at first throbbing. All were bilateral. The longer-lasting and more severe headaches soon lost this throbbing character and became "steady." If the experimental headache was not spontaneously likened to the previous complaint, the patient was directly questioned as to its character. Answers to all direct questions were evaluated according to the subject's total personality.

Three types of experiments were performed. In type A experiments, a sudden intravenous injection was given of approximately 0.00034 mg. of histamine per pound (0.00755 mg. per kilogram) of body weight. This dose was regulated according to the tabulation of subthreshold doses; for example, 0.04 mg. was given to patients weighing between 115 and 145 pounds (52 and 66 kg.). In type B experiments, 0.05 mg. of histamine phosphate was injected intravenously, irrespective of the subject's weight. Type C experiments consisted in first giving the proper subthreshold dose, according to the tabulation. If this failed to produce headache, the procedure was repeated at three minute intervals, with an increase of 0.01 mg. each time until headache occurred.

Procedures A, B and C were applied to three groups of subjects who at the time of the experiment were free from headache. The first group consisted of 36 patients subject to migraine headache. The diagnosis was made according to the criteria of recurrent, predominantly hemicranial headache, associated with visual disturbances, nausea and usually vomiting, occurring against a background of relative well-being but in the presence of a family history of migraine, epilepsy or

allergy.[7] The second group consisted of 23 patients afflicted with chronic recurrent headaches of the nonmigraine type; and the third group was composed of 15 subjects who stated that they had no tendency toward headache.

The results of these experiments were cross analyzed with respect to the occurrence, type, time of onset and duration of headache, the type of patient reacting with headache and the amount of histamine necessary to produce headache. Although the fallacies inherent in a statistical analysis of such a small series are realized, certain observations are sufficiently striking to warrant recording.

RESULTS

A total of 125 experiments was performed on 36 patients subject to migraine headache, on 23 patients subject to chronic, recurrent, nonmigraine headache and on 15 persons characteristically free of headache. The results are summarized in table 1.

Occurrence of Headache.—The small injections used in experiments A and B failed to produce headache in persons not previously subject

TABLE 1.—*Occurrence of Headache Following Intravenous Injection of Histamine*

	In 37 Patients Subject to Migraine Headache		In 23 Patients Subject to Nonmigraine Headache		In 15 Persons Not Subject to Headache	
Type of Experiment	Number of Experiments	Per Cent of Experiments Resulting in Headache	Number of Experiments	Per Cent of Experiments Resulting in Headache	Number of Experiments	Per Cent of Experiments Resulting in Headache
A	24	29	18	33	14	0
B	25	52	14	28	13	0
A and B	49	41	32	31	27	0
C	6	100	5	100	6	100
Total	55		37		33	

to headache. In contrast, headaches followed the same technic in a large number of the patients subject to chronic headache. Only slightly more headaches occurred in the total number of patients subject to migraine (41 per cent) than in those subject to other types of chronic headache (31 per cent). In the type A experiments there was no difference between the occurrence of headache in the groups with migraine and that in the group with nonmigraine headache. However, when the amount of histamine injected was increased (experiment B), headaches occurred in 52 per cent of the group with migraine and in only 28 per cent of the group with nonmigraine headache.

Type of Headache (table 2).—Among persons subject to migraine headache, 80 per cent of the experimental headaches were described as similar in character to migraine headache. Among those subject to nonmigraine headache, only 20 per cent of the experimental headaches were similar to the patient's habitual headache. This difference was

7. von Storch, T. J. C.: The Migraine Syndrome, New England J. Med. **217**: 247, 1937; M. Clin. North America **22**:689, 1938.

even more sharply demonstrated in the type B procedure. In these experiments, 92 per cent of those subject to migraine experienced a migraine headache, whereas in none of the group with the nonmigraine form did a headache develop similar to the previous complaint. Despite the similarity of the experimental headache to migraine headache, in none was the pain hemicranial, although in a few it was more severe on the side usually affected.

Type of Procedure Productive of Headache.—In the group with migraine headache both the frequency and the similarity to migraine of the headaches produced by the larger amounts of histamine in type B experiments were greater than in the type A experiments. This would be expected if histamine is a factor in the production of migraine headache. No such increase with larger doses occurred in the group with nonmigraine headache.

In the type C procedure, headache was "forced" by progressive increases in the amount of histamine used per injection. Naturally, all subjects finally experienced a headache. There was no significant

TABLE 2.—*Per Cent of Cases of Histamine Headache in Which the Condition Was Similar to Patient's Habitual Headache*

Type of Experiment	In 37 Patients Subject to Migraine Headache	In 23 Patients Subject to Nonmigraine Headache
A	57	33
B	92	0
A and B	80	20
C	67	60

difference between the group with migraine and that with nonmigraine headache with respect to the percentage of experimental headaches that were similar to the habitual complaint. The number of experiments was, however, too small to admit of any conclusions.

Amounts of Histamine Necessary to Produce Headache.—All doses were computed in hundred thousandths of a milligram per pound of body weight and then averaged for the various groups.

There was no difference in either the migraine or the nonmigraine group between the average dose of histamine producing headaches which were similar to and those producing headaches which differed from the subject's habitual complaint.

The average amount of histamine necessary to cause headache in those not subject to headache was distinctly greater (0.0004 mg. per pound [0.0009 mg. per kilogram] of body weight) than in either of the other groups subject to headache. As these doses were computed in such minute amounts, actual administration introduced a large error. When analyzed in detail, the figures indicated merely that a somewhat higher threshold dose was necessary to induce headache in those not subject to this complaint.

Onset and Duration of Headache.—Headaches appeared in the migraine patients and in those not subject to headache about ten seconds earlier than in those subject to nonmigraine headache. The headaches were shortest in those subject to migraine attacks and longest in those not subject to headache. This is to be expected, as the least amount of histamine was necessary to produce headache in the patients with habitual migraine and the largest amount in those not subject to headache.

There were no significant differences in the three types of patients with respect to time of onset of metallic taste, facial flush, subjective cranial fulness and throbbing.

COMMENT

These experiments justify the conclusion that patients who are subject to chronic headache are more susceptible to the type of headache produced by histamine than those who are not subject to headache. It is unlikely that this may be explained on a purely psychogenic basis by saying that these patients are familiar with headaches and hence interpret the cranial tension as headache. As a rule they did not complain as bitterly of headache when it was finally produced in the type C experiments as did those who were unfamiliar with this sensation.

On the basis of the known mechanism of headache produced by histamine, these results present several possible deductions. The first is that the branches of the carotid arterial tree are overly sensitive to histamine or similar vasodilator substances in patients habitually suffering from headache. As a corollary, it is also possible (but unproved) that accumulation, or periodic appearance, of such vasodilator substances is actually causative of these chronic recurrent headaches. On the other hand, vasodilatation may be the cause, by means of some entirely different mechanism, such as a neurogenic reflex or an allergic reaction. The second possibility is that the periarterial nerve plexus or its central receiving station (thalamus?) is hypersensitive in sufferers from headache. Thus, the stimulation of increased arterial pulsations caused by histamine would act on especially receptive neurons.

Irrespective of the mechanism productive of headache, these experiments tend to link histamine and migraine headache. There was a slight difference between the threshold for histamine headaches in subjects afflicted with migraine and that in subjects with nonmigraine headache, it being lower in the former. The type of headache produced offered better evidence that migraine headache is more similar to histamine headache than are the miscellaneous chronic types. However, no evidence was produced to show that any unilateral sensitivity to histamine was present in the vascular or nervous system of the migraine sufferer.

Nor did histamine produce an actual migraine attack, i. e., prolonged headache with nausea and vomiting, in patients subject to migraine.

The remainder of the analysis indicates that it is slightly easier to produce a headache with histamine in patients subject to migraine headache than in patients subject to other types of headache. When the evidence is considered as a whole, it adds another link to the chain of evidence connecting migraine and histamine headache. It implies that in the two forms the mechanism productive of pain is somewhat similar. Further investigations along these lines should prove fruitful.

CONCLUSIONS

1. Headache may be produced by sudden intravenous injection of minute amounts of histamine phosphate in from 30 to 40 per cent of patients subject to chronic recurrent headache.

2. The same procedure fails to cause headache in those who are characteristically free from this complaint.

3. Apparently the threshold for histamine headache is lower in persons subject to chronic recurrent headache than in those not so afflicted.

4. The threshold for histamine headache is somewhat lower in patients subject to migraine headache than in those subject to nonmigraine headache.

5. In patients subject to migraine attacks the type of headache produced by histamine is frequently similar to migraine headache.

6. In patients subject to other types of chronic recurrent headache the type of headache produced by histamine is only occasionally similar to the patient's habitual headache.

7. No evidence was discovered that the cranial vascular tree in patients subject to hemicranial migraine headache is unilaterally hypersensitive to histamine.

8. Further evidence has been presented linking migraine and histamine headache.

Dr. Halbert H. Leet rendered valuable assistance in the completion of this study.

INHIBITORY FUNCTIONS OF THE CORPUS STRIATUM

G. L. FREEMAN, PH.D.
AND
L. KRASNO, PH.D.
CHICAGO

Since the classic experiment of Wilson,[1] it has been generally agreed that electrical stimulation of the corpus striatum gives no primary motor effects. At the same time, clinical evidence has accumulated [2] which associates striatal dysfunction with impairment of motor activities originating elsewhere. The first adequate experimental proof of this relation was reported recently by Mettler, Ades, Lipman and Culler.[3] These investigators resorted to simultaneous activation of cortical and striatal motor centers, observing that "stimulation of the caudate nucleus in the course of cortically initiated movement produced inhibition of the movement . . . best described as a melting away of the cortical effect." The purpose of the present communication is to report an essential confirmation and extension of the evidence on experimentally produced striatal inhibition.

EXPERIMENTAL PROCEDURE

In 10 cats the caudate nucleus (and in 1 the putamen and claustrum as well) was systematically stimulated by faradic current from bipolar electrodes placed with the stereotaxic instrument. The cats were under anesthesia induced with pentobarbital sodium, and the strength of the stimulating current was kept at about 0.3 milliampere, as greater values would have caused "spread" effects from the internal capsule. Since no obvious changes in overt movement were produced by such stimulation alone, experimentation took the form of waiting for the appearance of "spontaneous" movements of the paws, face and tail, at which time the striatal tissue would be known to be stimulated. Occasionally the experimenter initiated movements by direct electrical stimulation of the cortex or by pinching the tail and then stimulating the caudate nucleus stereotaxically. In order to observe better the overlay effects of such stimulation, the hindlimbs in

---

Studies in Muscular Tension, series II, no. 15. The experiments reported in this paper were completed in 1938 at the Laboratory of Psychophysiology, Northwestern University.

1. Wilson, S. A. K.: An Experimental Research into the Anatomy and Physiology of the Corpus Striatum, Brain **36**:427-492, 1914.

2. Wilson, S. A. K.: The Old Motor System and the New, Arch. Neurol. & Psychiat. **11**:385-414 (April) 1924.

3. Mettler, F. A.; Ades, H. W.; Lipman, E., and Culler, E. A.: The Extrapyramidal System: An Experimental Demonstration of Function, Arch. Neurol. & Psychiat. **41**:984-994 (May) 1939.

some animals were rigidly fixed and the hamstring muscles partially dissected, with the tendons connected to levers writing on a smoked drum. Pneumatic recording systems permitted observation of effects of stimulation on breathing and bladder tension. A few records of toe pad sweating were obtained in terms of galvanic skin resistance. The motor cortex of two cats was removed some weeks before the acute experiments. The brain of each animal was sectioned to furnish a check on the locations of the stereotaxic needle. Such histologic examination showed that in the few instances in which stimulation produced phasic contractions of the limbs the capsular fibers had been approached.

RESULTS

The following paragraphs give condensed protocols for the 7 animals in which stimulation of the caudate nucleus yielded significant results.

CAT 2.—Excitation of the caudate nucleus was carried out over an area extending 21 to 17 mm. frontally from a transverse plane running through the external auditory meatus, 3 to 6 mm. laterally from the longitudinal fissure and 10 to 20 mm. ventrally, according to the lateral position of the electrode at that time. Capsular response was easily noted on the basis of certain ventral stimulations due to the phasic character of movements elicited. No overt responses of striatal origin were observed, but pinching the tail caused slight limb movements which were "held," or inhibited, by addition of the central stimulation. No particular somatic localization of these inhibitory effects was noted, though there appeared to be a tendency to greater "holding" of movements of the ipsilateral limbs.

CAT 3.—Stimulation of the caudate nucleus included an area extending frontally from 21 to 10 mm., laterally from 3 to 6 mm. and ventrally from 10 to 20 mm. Aside from occasional phasic (capsular?) responses in the ventral areas, the only observed effect was in modulating the activity of limbs already in "spontaneous" motion; that is, in depressing the activity in progress and in prolonging the relaxation time. In some instances stimulation was held beyond the usual half-second's duration while the experimenters attempted to induce movement by excitation of other origin. Movements induced by pinching the tail and flexing the legs appeared to be reduced and sometimes totally absent when the caudate nucleus was being excited. These effects were most pronounced on the ipsilateral side.

CAT 4.—The left caudate nucleus was stimulated over an area extending frontally from 21 to 17 mm., laterally from 1 to 6 mm. and ventrally from 10 to 17 mm. The effects of stimulation of these areas were compared with those resulting from direct stimulation of the internal capsule (over an area extending laterally 8 mm. and ventrally 18 mm.). The typical delaying effect on spontaneous activity of the limbs was observed during stimulation of the striatum; that activity was entirely different from the phasic movements elicited by stimulation of the internal capsule. Records of galvanic skin resistance from the front toe pads showed an average drop of 5,000 ohms (due to increased sweating) during capsular stimulation. Stimulation of the caudate nucleus immediately following or preceding capsular activation tended to cause reduction in the sweating. Most of the inhibitory action was noted to involve the forepaws, the effect being more pronounced as stimulation involved areas more frontally situated. Action potentials taken from the hindlimbs and forelimbs could not be interpreted, and this method was omitted from subsequent experiments.

CAT 6.—The right caudate nucleus and surrounding tissues were stimulated over an area extending 21 to 17 mm. frontally, 2 to 10 mm. laterally and 11 to 10 mm. ventrally. The right hamstring muscles were prepared for graphic recording, and the left sciatic nerve was bared. Stimulation of this nerve caused movements of the contralateral limb, which were clearly depressed or totally inhibited by stimulation of the caudate nucleus. Records of respiration and galvanic resistance from the front toe pads indicated depression of respiratory rate and activity of the sweat glands during striatal stimulation. These effects were most pronuonced when the stimulation was in the more frontal and lateral areas.

CAT 8.—The right caudate nucleus was stimulated with the stereotaxic electrodes over an area extending frontally 20 to 12 mm., laterally 2 to 6 mm. and ventrally 11 to 17 mm. Changes in tension in the right hamstring muscles, as well as bladder tension and sweating of the front foot pads, were recorded graphically. In general these three records tended to show similar trends in increase or decrease; that is, stimulation of the caudate nucleus caused reduction in tone of smooth and skeletal muscle as well in sweating. Micturition occurred

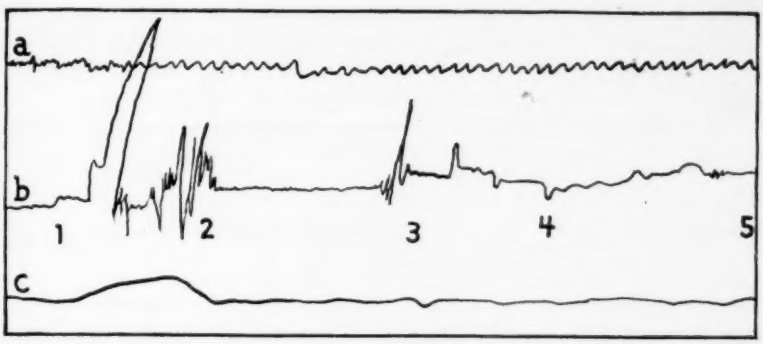


Fig. 1.—Inhibitory effect of striatal stimulation on activity induced by weak stimulation of sciatic nerve (cat 9; record retouched). *1* to *3* indicates stimulation of the sciatic nerve; *2* to *3*, stimulation of the corpus striatum also; *4* to *5*, striatal stimulation alone; line *a*, respiration; line *b*, action of the hamstring muscles, and line *c*, bladder tone.

after considerable striatal stimulation; as with many other observations, it could not be obtanied by restimulation of the same point, and there was little or no evidence for exact localization of the various inhibitory effects.

CAT 9.—The right motor cortex was removed four weeks before the experimental explorations so as to permit degeneration of the pyramidal tracts. Stimulation of the right caudate nucleus covered an area extending frontally 20 to 14 mm., laterally 3 to 6 mm. and ventrally 11 to 18 mm. Tension in the bladder and hamstring muscles, respiration and toe pad activity were recorded as for animals previously studied. Stimulation of the striatum alone caused some reduction in respiration and bladder tone but had little effect on the recorded hamstring tension. On the other hand, if the right hamstring muscle group was excited via the spinal level by a shock delivered to the left sciatic nerve, stimulation of the striatal tissue produced a decrease in its activity, as shown in figure 1. Instances of

apparent rise in hamstring tension during central stimulation were noted, but these were infrequent as compared with the inhibitory effects and might be assumed to be due to inhibition of some antagonistic muscle action.

CAT 10.—Both motor cortices had been removed four weeks before the experiments. The animal was placed under light anesthesia induced with pentobarbital sodium, which permitted the occurrence of many spontaneous movements of the limbs. The area of stimulation extended frontally from 20 to 14 mm., laterally from 3 to 6 mm and ventrally from 12 to 18 mm. The picture furnished by the various graphic records, as well as by gross observations of limb movements, now became clear. With the exception of occasional "silent areas," excitation of the caudate nucleus caused marked reduction of spontaneous movements, especially on the ipsilateral side. Often, as soon as striatal stimulation was introduced there was marked reduction in limb activity and bladder tension; as shown in figure 2, when the needle was removed the spontaneous limb movements again appeared and the bladder regained its normal tone. Since all parts stimulated gave at times the inhibitory effect, it is impossible to state the degree of somatic localization.

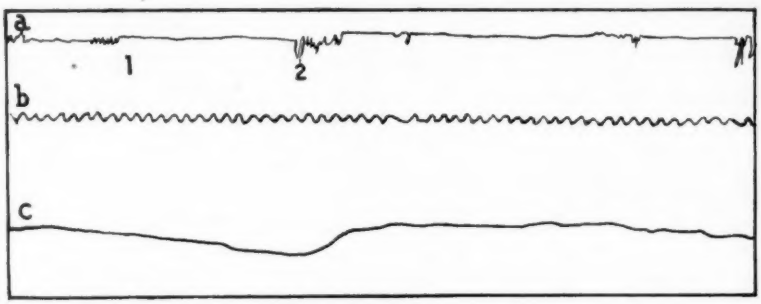


Fig. 2.—Inhibitory effect of striatal stimulation on "spontaneous" motor activity (cat 10; record retouched). *1* to *2* indicates stimulation of the corpus striatum; line *a*, action of the hamstring muscle; line *b*, respiration, and line *c*, bladder tone.

COMMENT

It may not be assumed that the effects mentioned in the protocols could be obtained from the spread of excitation to the internal capsule, as the strength of current necessary to stimulate these motor fibers is much greater than that ordinarily used on the cellular mass of the corpus striatum. Furthermore, the responses of the capsule have a shorter latent time and are primarily contralateral rather than ipsilateral. In animals with capsular fibers degenerated, after removal of the motor cortex, similar inhibitory and "holding" effects on spontaneous movements were noted.

The results in these experiments thus confirm and extend those of Mettler, Ades, Lipman and Culler, who found that excitation of the corpus striatum inhibits movements initiated by cortical stimulation. We have shown that similar tonic modulation of the phasic response may occur when the phasic excitant is of lower (spinal) origin. Moreover,

when suitable recording methods are employed striatal stimulation is seen to cause apparent reduction in bladder tension and skeletal muscle tone, depression of respiration and decrease in activity of the sweat glands. The influence on skeletal muscle tone is largely ipsilateral and shows little somatic localization within the caudate nucleus, although the possibility of such localization still exists. We cannot at present fully explain the physiologic principles underlying these inhibitory effects, but suggest that they may be regarded as "conditioning" phenomena—a tonic extrapyramidal "set" of the motor neurons of the final common path with reference to phasic activity of the corticospinal system.

CONCLUSIONS

1. Stimulation of the caudate nucleus inhibits spontaneous movements of the skeletal muscles, probably induced by the corticospinal system. The effect is best noted on the ipsilateral side.

2. Stimulation of the caudate nucleus inhibits bladder tone and tends to depress respiration and reduce activity of the sweat glands.

3. Little evidence for somatic localization of these effects within the corpus striatum has been found.

ELECTROENCEPHALOGRAPHIC STUDIES OF INJURY TO THE HEAD

HERBERT H. JASPER, D. ès. Sc.

JOHN KERSHMAN, M.D.
AND
ARTHUR ELVIDGE, M.D.
MONTREAL, CANADA

Berger's original observations that the electroencephalogram provided a sensitive indicator of certain pathologic conditions of the brain has received abundant confirmation. Slow "delta" waves, below the normal alpha frequency of 8 to 12 per second, appear from cortical tissue undergoing irreversible degenerative changes or from a reversible depression of cortical function, such as occurs with low blood sugar,[1] with certain drugs [2] or with normal sleep.[3] The electroencephalogram has also been found useful in the localization of certain focal cortical lesions.

Injuries to the head produce both reversible and irreversible changes in cerebral function. Clinical and pneumographic (roentgen) examinations do not always give a clear picture of the nature, extent or localization of cerebral damage. The present study is concerned with the results of electroencephalographic examinations of patients who have suffered various degrees and kinds of injury to the head. The attempt is made to correlate the electroencephalographic findings with the results of other forms of clinical examination.

DEFINITIONS

In order to clarify the terminology used in the present report, it is felt necessary to define what is meant by cerebral concussion, cerebral contusion, and cerebral laceration.

Read before the Section on Nervous and Mental Diseases at the Ninety-First Annual Session of the American Medical Association, New York, June 12, 1940.

From the Department of Neurology and Neurosurgery, McGill University, and the Montreal Neurological Institute.

1. Hoagland, R.; Rubin, M. A., and Cameron, D. E.: Electrical Brain Waves in Schizophrenics During Insulin Hypoglycemia and Recovery, Am. J. Physiol. **120**:559-570, 1937.

2. Gibbs, F. A.; Gibbs, E. L., and Lennox, W. G.: Effect on the Electroencephalogram of Certain Drugs Which Influence Nervous Activity, Arch. Int. Med. **60**:154-166 (July) 1937.

3. Loomis, A. L.; Harvey, E. N., and Hobart, G.: Electrical Potentials of the Human Brain, J. Exper. Psychol. **19**:249-279, 1936.

Cerebral Concussion.—By this term is meant that condition which gives rise to a lapse of memory or a short period of unconsciousness; it is the immediate result of an injury to the head, the physiologic and pathologic explanations for which are as yet undetermined. This state is typically transient and is not necessarily accompanied by other objective neurologic signs of disturbance in the brain. Neither is the condition consistently associated with increase or decrease of spinal fluid pressure, and the fluid may be free from red blood cells.

Cerebral Contusion.—By this term is meant gross bruising or traumatic hemorrhagic softening of brain tissue, which may be seen at operation or at postmortem examination. Judged clinically, cases are included in which there are definite neurologic signs, usually of a focal character. With cerebral contusion there is usually associated some degree of subarachnoid bleeding. In some of the cases in this study marked subarachnoid bleeding without neurologic signs was considered evidence of contusion.

Cerebral Laceration.—This term signifies an actual gross rupture of continuity of brain tissue. In civilian life this is usually dependent on the protrusion of a depressed fragment of bone. Patients with such injuries may or may not show red blood cells in the spinal fluid on lumbar puncture.

Subarachnoid bleeding in any quantity can be determined by comparing the red cell counts on the first and last specimens of fluid withdrawn on lumbar puncture. In the present article 50 cells per cubic centimeter is used as the minimum significant quantity.

CASE MATERIAL AND METHODS

Sixty-four patients are included in this survey. Of these, 37 were admitted to the hospital with acute injuries to the head, and 23 were patients with more chronic disorders who presented some diagnostic problem associated with a previous injury to the head. Four patients are included who had intracerebral vascular lesions which, though not directly associated with an injury to the head, presented similar diagnostic problems.

There were 47 male and 16 female patients, the preponderance of men being doubtless due to their greater industrial hazards. The ages varied from 6 weeks to 58 years.

The clinical diagnosis in these cases is shown in the accompanying tabulation.

Clinical Diagnosis	No. of Cases
Cerebral concussion	28
Questionable concussion	6
Cerebral contusion	16
Cerebral laceration	6
Linear fracture of the skull	15
Compound and comminuted fracture of the skull	8
No fracture	37
Subarachnoid hemorrhage	26
Post-traumatic neurosis	3
Post-traumatic psychosis	2
Subdural and epidural hematoma and effusion	8

In this survey we have not considered patients with late, focal, post-traumatic epilepsy because they are being made the subject of a special study. Five patients are included who had immediate post-traumatic convulsions within a few days and 1 in whom convulsions were associated with a subdural hematoma.

Electroencephalographic Studies.[4]—Of the 37 patients admitted to the hospital with acute injuries to the head, 5 had electroencephalograms either immediately

4. Electrogram will be used as an abbreviation for electroencephalogram in this report.

after the injury or on the same day. An additional 10 were examined within forty-eight hours. Twelve more patients were studied within the first week and then within twenty-one days of the original accident. There were 23 patients who were studied as diagnostic problems and had their first electroencephalogram more than twenty-one days after the original injury to the head.

With regard to the follow-up study of these patients, 15 had two or more electroencephalographic examinations, and 1 of these had ten. Of the 27 patients who were studied within the first week after the injury, there were 9 the subsequent course of whose disease was followed for periods varying from one to five months.

Electroencephalographic Technic.—Electrograms were recorded from the prefrontal, frontal, central, parietal, occipital and temporal regions of the head according to standard placements on the scalp as measured from reference points on the

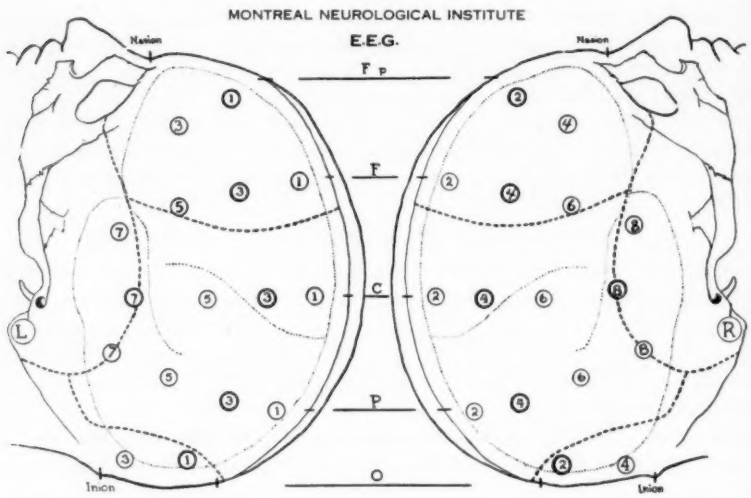


Fig. 1.—Schematic representation of the points on the surface of the head at which electrodes were placed in making electroencephalograms. From eight to fourteen leads in different regions over the two hemispheres were used.

skull. Small silver cups (with an inside diameter of about 3 mm.) attached to the scalp with collodion were used as electrodes, the contact to the skin being made through an electrode jelly. Eight to fourteen leads in different regions over the two hemispheres were used in individual patients. The positions for the electrodes were numbered, so as to facilitate reference to any particular region of the head, as shown in figure 1.

In adults, electrograms were taken routinely from positions *3* and *4* in the frontal, central and parietal lines, with positions *1* and *2* in the prefrontal and occipital regions and *C7* and *C8* in the left and right temporal regions, respectively (heavy circles, fig. 1). In children, positions *1* and *2* were used instead of positions *3* and *4* and positions *C5* and *C6* instead of *C7* and *C8* because of the smaller size of the head. It cannot be assumed that these standard placements on the scalp

assure constant positions over certain areas of the brain in all patients, but it is convenient to have numbered positions which are reproducible at least for a given patient.

The same positions on the head were used for both monopolar and bipolar recording. For the so-called monopolar record from a single lead on the surface of the head, the ear lobes, indicated by *R* and *L* on the chart, were used for the reference electrode. Bipolar records were obtained by using two adjacent positions, either in an anteroposterior direction (for example F3 to C3) or in a mediolateral direction (for example, C2 to C4). Simultaneous bipolar and monopolar records were often taken of the same region of the head because of important differences obtained between the two methods of recording. The bipolar leads, spaced about 3 cm. apart, recorded potentials from local surface cortical areas, while the monopolar leads picked up potentials from deeper lying and more distant regions. The presence of an inert conducting medium, such as a subdural hematoma, between the skull and the cortex would tend to short-circuit cortical potentials to closely spaced bipolar leads on the scalp, while monopolar leads recorded the potentials through the fluid from the cortex beneath. Silent regions recorded from bipolar leads served to indicate a subdural effusion or hematoma.

The recording system consisted of four independent condenser-coupled amplifiers operating electromagnetic ink-writing oscillographs. The patients were placed in a soundproof, electrically shielded room throughout the examinations. A trained observer sat with the patient to signal all movements and to report the general condition of the patient.

ELECTROENCEPHALOGRAPHIC AND CLINICAL OBSERVATIONS

The types of abnormality observed in the cerebral electrical activity following injury to the head were similar to those which have been found associated with other forms of cerebral lesions.[5] The chief forms were the following.

Delta Activity.—The most common type of abnormality was the delta activity obtained either from a restricted area or diffusely from all regions of the head. This delta activity consisted of slow waves at frequencies of from less than 1 to 6 or 7 per second. Often the waves were irregular, recurring in a more or less random fashion, so that it was difficult to assign any particular frequency to the disorganized patterns of slow waves obtained. In some patients, however, the activity was organized in bursts of slow waves of larger amplitude at definite frequencies of 2 to 4 per second.

5. (*a*) Walter, W. G.: Critical Review: The Technique and Application of Electroencephalography, J. Neurol. & Psychiat. **1**:359-385, 1938. (*b*) Case, T. J., and Bucy, P. C.: Localizations of Cerebral Lesions by Electroencephalography, J. Neurophysiol. **1**:245-261, 1938. (*c*) Williams, D., and Gibbs, F. A.: Electroencephalography in Clinical Neurology: Its Value in Routine Diagnosis, Arch. Neurol. & Psychiat. **41**:519-534 (March) 1939.

The amount and type of delta activity were found to be the best single measure of the severity of cortical damage.[6] In cases of the most severe injury the electroencephalograms were composed entirely of delta waves, mainly of the slower random type, with no trace of normal alpha rhythm.

Alpha Activity.—In some patients the alpha rhythm appeared prominent after injury to the head but was disorganized and irregular. Its frequency did not show the usual stability but shifted between 7 and 11 per second. There was poor regulation of amplitude, with bursts of waves of large amplitude and irregular peaks, separated by quiet periods. Such disorganization was usually associated with some underlying delta activity.

Usually the amount of alpha activity (8 to 12 per second rhythms) was inversely related to the amount of delta activity. Little or no alpha rhythm and a large amount of delta rhythm occurred with severe injuries. Normal persons vary greatly, however, in the amount of alpha rhythm, so that this was not considered a certain indication of abnormality unless combined with asymmetric recordings from homologous regions of the head—as when alpha rhythm was obtained from the right and not from the left parieto-occipital region.

Epileptiform Activity.—Electrograms which could be called clearly epileptiform[7] were rare in this series of cases. In 3 cases bursts of the "petit mal" type of 3 per second spike and slow wave pattern were observed late in the course of recovery. In 1 case there was the multiple spike picture typical of the "grand mal" type of discharge. In 1 case bursts of sharp waves at a frequency of about 6 per second ("psychomotor") occurred several months after a severe injury which was followed by marked changes in personality. Bursts of smooth 3 per second waves of fairly large amplitude were common, but it was thought that there was not sufficient justification for calling them epileptiform, although they may well have represented a transient disturbance in cortical function similar to that reported for certain mild epileptoid conditions.

---

6. The relation between the frequency of delta activity and the severity of acute injury to the head is the same as reported by Walter,[5a] who found that the slower waves corresponded to more acute and severe degenerative processes in the vicinity of a malignant tumor, while waves of alpha frequency might be obtained around a slowly growing glioma or meningioma.

7. Gibbs, F. A.; Gibbs, E. L., and Lennox, W. G.: Cerebral Dysrhythmias of Epilepsy, Arch. Neurol. & Psychiat. **39**:298-314 (Feb.) 1938.

The kind and localization of the abnormality in the electroencephalogram bore a fairly consistent relation to other clinical observations, and in some cases important additional information was provided. The nature of the results obtained with different kinds of patients is illustrated in the following case histories.

REPORT OF CASES

CASE 1.—*Mild local injury with complete recovery. Diagnosis: Cerebral concussion with mild subarachnoid hemorrhage.*

M. B., a woman aged 24, was knocked down by a truck and struck the right side of her head. There was no history of unconsciousness, but the patient felt slightly drowsy, and there was a short period of retrograde amnesia. On examination one hour later, there were a hematoma over the right side of the forehead and

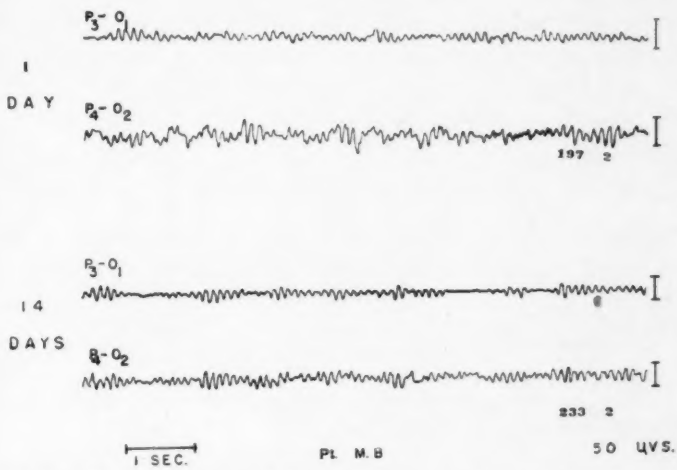


Fig. 2 (case 1).—Electroencephalograms from a patient with mild local trauma. The upper record was made the day after the injury; the lower, which is normal, was made fourteen days later.

abrasions of the face. The left pupil was slightly larger than the right, with a varying and sluggish response to light, and there were generally hyperactive deep reflexes, though the superficial reflexes were normal. There were about 500 red blood cells per cubic millimeter of cerebrospinal fluid; roentgen examination revealed no fracture.

The electroencephalogram on the day following the injury (fig. 2) showed definite irregularity of the alpha rhythm from the right parieto-occipital region, with delta waves of low amplitude. Records from other regions of the head were normal. Although the subcutaneous hematoma was on the right side of the forehead, presumably indicating the site of direct injury to the head, the electroencephalographic abnormality was in the occipital region, a location for a contrecoup.

Fourteen days later a normal electroencephalogram was obtained, as shown in the second record of figure 2.

CASE 2.—*Mild generalized injury. Diagnosis: Questionable concussion.*

M. G., a girl aged 4 years, was struck by an automobile. She was not unconscious, but was drowsy for a short time and vomited once, two hours after admission. Physical examination gave essentially normal results. There were 37 red blood cells per cubic millimeter of cerebrospinal fluid. Roentgen examination revealed no fracture.

The electroencephalogram, taken a few hours after the injury (fig. 3), showed diffuse delta activity, most marked in the occipital regions and more pronounced on the right side than on the left. Occasionally there were bursts of 3 per second slow waves, resembling those seen in petit mal epilepsy but without the spike component. Normal alpha waves were superimposed on the delta waves.

Four days later the alpha rhythm was better organized and more regular. There was less generalized delta activity, and it was of lower amplitude and more prominent in the right occipital region.

In these cases the clinical evidence of cerebral injury was minimal, but the electroencephalogram showed definite, though relatively mild, abnormalities, most of which were reversible, as shown by the relatively

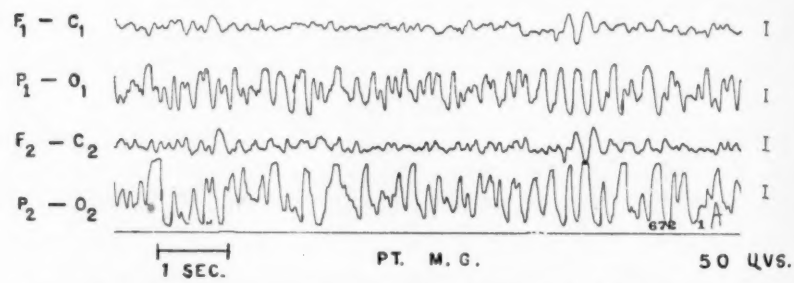


Fig. 3 (case 2).—Electroencephalogram from a patient with mild general trauma, recorded a few hours after the injury.

rapid return toward the normal. Case 1 illustrates the possibility of demonstrating a mild contrecoup injury to the brain, with complete recovery, in the absence of localizing neurologic signs.

CASE 3.—*Moderately severe, generalized injury, followed by electrographic evidence of spike and slow wave ("petit mal") activity. Diagnosis: Cerebral concussion and contusion, with subarachnoid hemorrhage and fracture of the skull.*

W. T., a girl aged 4, was struck by an automobile, after which she was unconscious for about ten minutes and then drowsy. On examination, a hematoma was observed over the right side of the occiput, and the child was drowsy and irritable. The abdominal reflexes on the left were diminished, and there was a coarse tremor of the head. There was internal strabismus on the left side, which disappeared after lumbar puncture. The spinal fluid contained 50,000 red blood cells per cubic millimeter, and the roentgen examination demonstrated a linear fracture in the right occipital region.

Electroencephalograms were taken on the following day (fig. 4), when the patient was still restless and irritable. Physical examination otherwise gave

essentially normal results. Continuous 1 to 2 per second delta waves, of moderate amplitude, were present. They were more prominent posteriorly, especially on the right side. There was also some poorly regulated slow alpha rhythm.

The electrogram was repeated forty-four days later. At this time the patient was regarded as clinically normal. There was some return of the alpha rhythm, with much less random, irregular delta activity. From time to time, however, bursts of slow waves occurred and were accompanied by some sharper potentials (fig. 4) resembling those in subclinical petit mal attacks. These appeared mainly from posterior regions of the head. Although judging from the electroencephalogram, some generalized recovery of function had occurred, a definite residuum of abnormality, some of it epileptiform, was present.

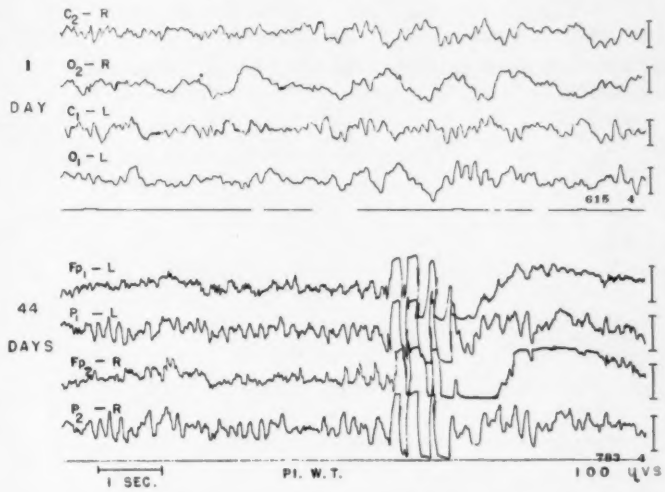


Fig. 4 (case 3).—Electroencephalograms from a patient with generalized trauma. The upper record was made the day after the injury, the lower forty-four days later.

CASE 4.—*Moderate injury, with clinical recovery and disappearance of 3 per second waves. Diagnosis: Concussion with slight subarachnoid hemorrhage.*

L. F., a boy aged 11, sustained an injury to the head; he was unconscious for several hours and drowsy on the following day. There were a hematoma in the left frontal region, weakness of the left arm and slight left hemiparesis. Roentgen examination showed a possible linear fracture of the left frontal bone. The cerebrospinal fluid contained 50,000 red blood cells per cubic millimeter. A pneumogram ten days after the injury showed diffuse enlargement of the right ventricle, with questionable enlargement of the left.

The first electrogram was taken twelve days after the injury, at which time the deep reflexes on the left side were still accentuated. The record showed almost continuous delta waves of low amplitude, chiefly from posterior regions of the

head, with some alpha rhythm. The delta waves displayed a tendency to occur in bursts of 3 per second smooth waves, most prominent on the right side.

Twenty-two days later the bursts of slow waves had completely disappeared. Some occasional delta waves of low amplitude were still present, and there was an increase in the amount of normal alpha activity, which, however, was of low amplitude. The patient was judged to be clinically normal at this time.

One hundred and twenty-two days later the alpha potentials had become more regular; their amplitude was greater, and only a few random delta waves occurred.

This case illustrates that even after a moderately severe cerebral injury and the appearance of bursts of 3 per second delta waves there can be an almost complete recovery as judged by the electroencephalogram. The clinical recovery seemed to precede the electroencephalographic recovery.

In more severe cerebral injuries the alpha rhythm completely disappears, and the electrogram consists of continuous irregular, random

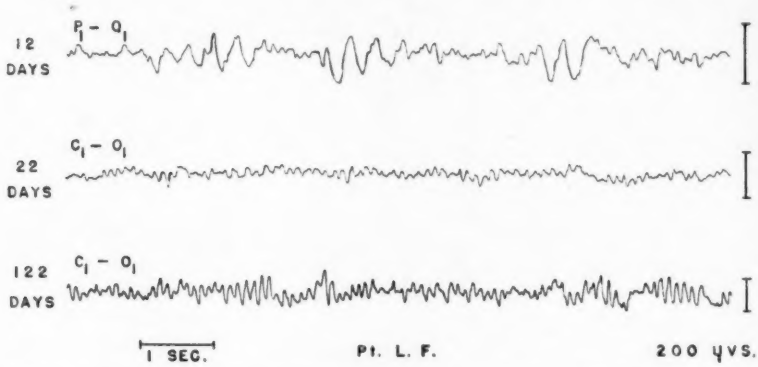


Fig. 5 (case 4).—Electroencephalograms from a patient with moderate trauma. The first record was made twelve days after the injury, the second twenty-two days later and the third one hundred and twenty-two days later.

slow delta waves, varying in frequency from 1 to 4 per second. Such activity occurs locally in cases in which there is cerebral laceration associated with a depressed comminuted fracture of the skull and may persist after the generalized effects of concussion have disappeared, thus indicating the localization of most severe injury. This is illustrated by the following case.

CASE 5.—*Severe trauma with cerebral laceration. Diagnosis: Laceration of dura and brain; right subaponcurotic hematoma; left subdural effusion; marked subarachnoid hemorrhage; immediate post-traumatic convulsive state.*

B. V., a boy aged 5½, fell off a wagon, striking the right side of his head on the pavement. He was unconscious for about twenty-four hours. On examination shortly after the injury, there were a large hematoma on the right side of the head and incomplete left hemiplegia, with some difficulty of movement of the right

side. Twitching of the right arm and leg was observed. Roentgen examination revealed a comminuted depressed fracture of the right parietotemporal region, with linear extension around the posterior aspect of the skull to the right side.

At operation the comminuted depressed fracture was elevated, débridement was carried out, the softened lacerated brain was removed and the dura sutured in the right parieto-occipital region.

An electroencephalogram was taken twelve days after the operation. On the right side no normal alpha rhythms were recorded. The electrogram (fig. 6) showed continuous irregular, random delta waves, varying in frequency from less than 1 to 2½ per second, which were highest in amplitude and most irregular in the right parieto-occipital region (site of cerebral laceration and débridement). On the left side a moderately regular alpha rhythm was obtained anteriorly, but posteriorly, in the regions homologous to the site of the most severe injury, there was a moderate amount of random delta activity, with some traces of alpha rhythm superimposed.

Subsequent electrograms of this patient, the last examination being twenty-five days after the accident, showed persistence of the slow random delta waves and no alpha rhythm in the right parietal region. Recordings from other regions of the

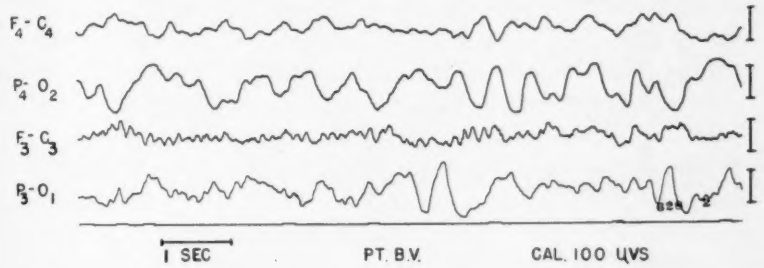


Fig. 6 (case 5).—Electroencephalogram from a patient with severe generalized trauma of the right hemisphere and of the posterior portion of the left hemisphere, taken twelve days after an operation for elevation of the comminuted depressed fracture and débridement.

head demonstrated a definite tendency to return to normal, with an increasing amount of alpha and a diminishing amount of delta activity.

In some cases the amount of generalized cerebral damage is so severe that normal rhythms are completely absent in all regions of the head and are replaced by continuous random delta activity. The following case will serve to illustrate a severe injury, with parallel clinical and electroencephalographic improvement over a period of four months.

CASE 6.—*Severe generalized injury. Diagnosis: Profound cerebral concussion and contusion, involving also the brain stem, marked subarachnoid hemorrhage; primary post-traumatic optic atrophy; cerebral atrophy, and convulsive state.*

A. M., a boy aged 7 years, was struck by an automobile and remained unconscious for several weeks. On admission to the hospital two days after the injury he was deeply comatose. There was rigidity of the neck, and on stimulation decerebrate spasms occurred. The deep reflexes were absent; the right plantar response

was of extensor type, and the abdominal reflexes were absent. The right pupil was dilated and fixed; the left was smaller and reacted to light directly but not consensually.

The first electrogram (fig. 7), recorded on the fourth day after injury, consisted of continuous irregular delta waves of moderate amplitude from all regions of the head, varying in frequency from 1½ to 3 per second, with no background alpha rhythm. The samples shown in figure 7 were obtained from the left frontal (upper line) and the left parieto-occipital region.

On the nineteenth day, when the patient was beginning to recognize his parents and was responding to loud noises by opening his eyes, the electroencephalogram

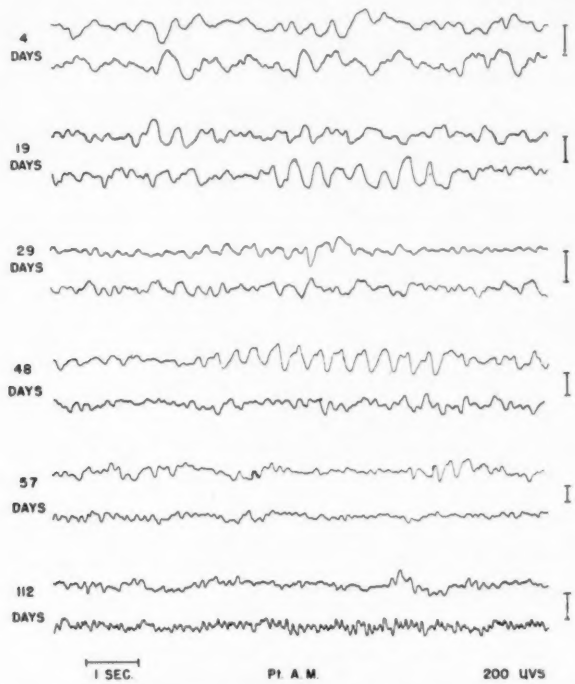


Fig. 7 (case 6).—Electroencephalograms from a patient with severe trauma. The records were made four, nineteen, twenty-nine, forty-eight, fifty-seven and one hundred and twelve days, respectively, after the injury.

showed a definite increase in the amplitude, regularity and frequency of the delta potentials, with occasional bursts of 4 to 5 per second waves.

On the twenty-ninth day there was further diminution in the amount and irregularity of the random delta activity, with an increase in the appearance of regular 5 per second rhythms. Clinically, the patient was responding to painful stimuli by crying. The eyes blinked when objects were presented; both pupils were dilated and reacted to light and in accommodation.

Forty-eight days after the accident the boy was moving his limbs spontaneously and laughing in response to appropriate stimuli. The electrogram showed a fairly regular 6 per second background activity, with some random delta waves. In both

frontal regions bursts of regular 2 to 3 per second delta waves of high amplitude occurred, similar to those in what has been termed subclinical epileptiform activity.

The next electrogram, on the fifty-seventh day, showed for the first time a fairly regular 7 to 8 per second alpha rhythm in the occipital region, with, however, frequent periods of 5 to 6 per second waves. Bursts of 2 to 3 per second delta waves still occurred in both frontal regions, though not as frequently.

The last examination of this patient to date was one hundred and twelve days after the injury. At this time he was alert, cooperative and coherent, but there was some residual weakness of the right arm and leg. There was now much more alpha rhythm from the parieto-occipital region on both sides, though the frequency was poorly regulated, varying from 7 to 10 per second. Some delta waves of low amplitude were still present, occasionally occurring in bursts of 3 per second in the frontal regions. These abnormalities were somewhat more pronounced in the left hemisphere.

This case shows clearly the manner in which the cerebral potentials return to normal after severe injury. Beginning with continuously irregular, random delta waves of low amplitude, they become more regular in both frequency and amplitude. There is a gradual increase in frequency, and gradually alpha rhythm makes its appearance. As recovery proceeds, the amount of alpha activity increases and the delta activity diminishes. Throughout there is a constant correlation between the clinical improvement and the tendency of the electrogram to return to normal.

The relation between the bursts of 2 to 3 per second delta waves, which have been described in several cases, and petit mal epilepsy is a question we cannot settle with available data. Since these waves seem to represent a transient phase in recovery not associated with any clinical epileptic symptoms, they cannot be called definitely epileptic.

Five patients in our entire series had convulsive seizures shortly after a severe injury to the head. One of these, from whom a good electroencephalogram of the attacks was obtained, will be reported on in some detail.

CASE 7.— *Epilepsy immediately following trauma. Diagnosis: (1) Linear fracture of the skull, in the right occipito-parietal region, with probable fracture of the base; (2) cerebral concussion; (3) cerebral contusion and compression, with marked subarachnoid hemorrhage; (4) small lacerations with diffuse hematoma; (5) slight subdural effusion; (6) post-traumatic convulsive state.*

L. M., a woman aged 24, when riding at night in an automobile fell through the open door, striking the back of her head on the pavement. She was not unconscious immediately but was somewhat stunned and bled profusely from a wound over the back of the head and from the nose. Within forty-five minutes of the accident discoloration and swelling of both orbits appeared. The patient refused medical treatment and went to bed. She vomited several times during the night, and was irrational in the morning when admitted to the hospital.

Examination.—On admission the patient complained of headache and resented movement. The eyelids were blue-black and swollen. There were two puncture wounds in the right occipitoparietal region, with extensive diffuse hematoma of the scalp and multiple abrasions of the trunk and limbs. There were slight stiff-

ness of the neck and a subconjunctival hemorrhage on the right side. Plantar flexion was normal on the right and less definite on the left; the abdominal reflexes were not obtained. The blood pressure was 120 systolic and 80 diastolic. Examination otherwise gave essentially normal results.

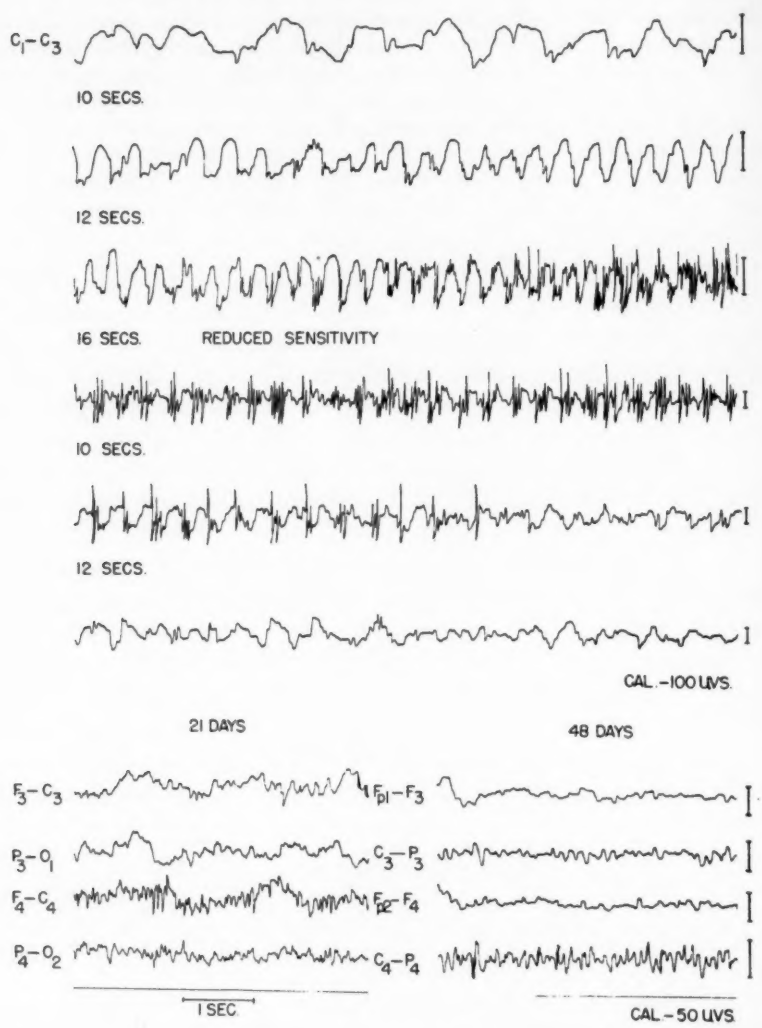


Fig. 8 (case 7).—Electroencephalograms from a patient who had grand mal attacks after injury. The first record was made three days after the injury, during an attack, the second twenty-one days and the third forty-eight days after the injury.

Six hours later the patient was uncooperative and disoriented. The right optic disk was normal, but the left optic disk was slightly blurred along the nasal edges. The left pupil was larger than the right; both reacted to light; subconjunctival hemorrhage covered the outer half of the right eye. There was no stiffness of the neck, and movement of all extremities was free. The knee jerks were equally

hyperactive. There were slight ankle clonus, more pronounced on the right, and plantar flexion bilaterally.

Lumbar puncture showed that the spinal fluid was bloody and under a pressure of 250 mm. of water. Roentgen examination showed a long linear fracture in the right parietotemporal region.

The patient complained of severe headache. Irrational periods alternated with drowsiness. There were involuntary twitching movements of the left leg, sometimes involving the left shoulder.

Course.—On the second evening following the accident a severe convulsive seizure occurred. The blood pressure fell to 64 systolic and 50 diastolic and the pulse rate to 60, the pulse becoming weak and uneven; the attack lasted one minute. On the following morning, the third day after the injury, the patient began to have grand mal attacks about every ten minutes. The first attack involved the left side, but subsequent attacks appeared to begin with choking sounds, sometimes with the head and eyes turning to the right, and clonic movements of all extremities. It was at this time that the first electroencephalographic examination was carried out.

Electroencephalograms.—When the patient was quiet, delta waves at a frequency of about 1 per second and of fairly large amplitude, appeared from all regions of the head, as shown in the upper line of figure 8. These slow waves then gradually increased in frequency to about 3 per second, when sharp spikes appeared superimposed on them and the clinical seizure was seen to begin. The spikes then increased in number and amplitude until they dominated the picture for about one minute before dropping out, leaving only delta activity of lower amplitude. The cycle would repeat itself about every five or ten minutes. The epileptiform activity began from the left side, and the seizures were mainly on the right side at this time.

Operation.—With the patient under anesthesia induced with ether and avertin with amylene hydrate a right subtemporal craniotomy and right and left parietal trepanations were performed. A small subdural effusion was observed on each side. The temporoparietal suture line was found to be separated, and some loose fragments of bone lay along its course; in addition, there was a traumatic rupture of the dura in the right temporal region. Every portion of the brain exposed through the several openings, including the point of traumatic rupture of the dura, showed discolored cerebral tissue which appeared to be contused, so that the diagnosis of multiple cerebral contusions was verified in this case.

Subsequent course.—On the following day the patient was again extremely restless, uncooperative and aphasic. During the day convulsions reappeared, gradually becoming more frequent; they ceased only after the administration of avertin with amylene hydrate. Attacks recurred during the next two days, but on July 22, four days after the operation, the patient was decidedly better, though there was obvious motor aphasia and she was still somewhat restless. Steady improvement continued, so that fourteen days after the operation she was able to write a letter with only two wrong words.

Subsequent electroencephalograms.—Twenty-one days after the injury a second electroencephalogram was taken. A sample record is shown at the bottom of figure 8. Random delta waves, at about 1 per second, were still appearing occasionally from posterior regions of the head, but a trace of normal alpha rhythm was also present. The epileptiform spikes of large amplitude were no longer present, but there was a local region over the right central region of the head which gave rise to sharp spikes resembling a subclinical "grand mal" type of epileptic activity. This was over the region of most severe damage to the brain, where there was laceration of the dura, and was also near the area from which the first convulsive movements may have arisen.

The final electroencephalographic examination was made forty-eight days after the injury, when the patient showed no important residual neurologic signs. There was a marked decrease in delta activity at this time, and a normal alpha rhythm was becoming organized from parieto-occipital regions on both sides, as shown in the lower record at the right of figure 8. There were no signs of epileptic activity at this time. Although there was a significant amount of residual abnormality in the electroencephalogram the degree of recovery relative to the original severity of injury was remarkable.

SUBDURAL HEMATOMA AND EFFUSION, EPIDURAL HEMATOMA AND INTRACEREBRAL HEMORRHAGE

A subdural collection of fluid or blood is manifest in the electrogram by a relatively quiet or silent record from closely spaced bipolar leads on the scalp directly over it. The fluid separating the cortex from the skull, being a good conducting medium, acts as a short circuit for cortical potentials, so that they become too small to detect with bipolar leads on the scalp. It is necessary, however, that the area of collected fluid be large enough not to allow potentials from its borders to reach one of the two recording electrodes. In practice this would require the electrodes to be placed within an area about 6 cm. in diameter before a reasonably silent electrogram could be expected.

When the subdural effusion or hemorrhage is bilateral it is sometimes difficult to determine whether the absence of cortical potentials is due to this added substance or to other possible causes. When the bipolar records are quiet relative to the monopolar records of the same area, it is at least suggestive evidence of some inert conducting mass between the skull and the cortex on both sides, especially when combined with clinical indications. An example of two quiet areas from bipolar leads over the right and left parietal regions of the head, with delta waves from the monopolar lead to the same region, is shown in the first example of figure 9. In this case a large bilateral subdural hematoma was evacuated immediately after the electrographic examination.

If the subdural fluid is present only on one side it is more easily detected by the asymmetry in amplitude of simultaneous records from bilaterally homologous regions. This is illustrated in the second record of figure 9, which shows a normal beta rhythm from the right central region, with a flat line from the left central region. A large subdural hematoma was found beneath the left central region of the head. Electrographically, an epidural hematoma behaves in the same way as a subdural one.

In contrast to the subdural hemorrhage, an intracerebral hemorrhage may often be detected and localized by the delta activity arising from surrounding gray matter which has been damaged by the presence of the hemorrhage. An example of a traumatic intracranial hemorrhage correctly localized by the electroencephalogram is shown in figure 10.

The phase reversals of the delta activity occurred on the cortex lying immediately over the lesion. The presence of some delta activity of lower amplitude from monopolar leads to the opposite side suggested a

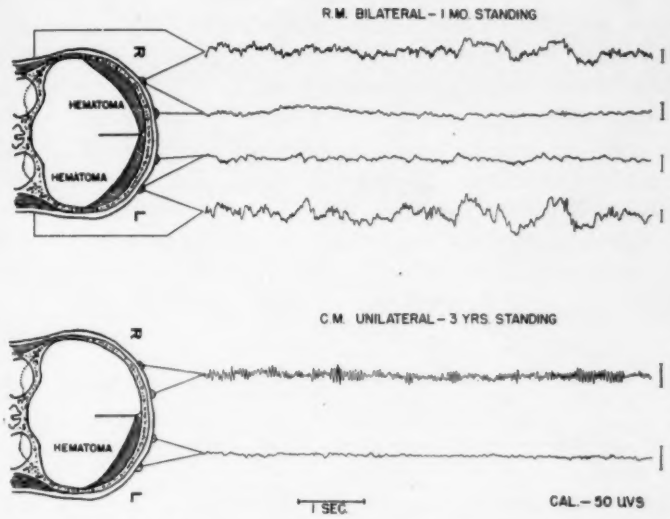


Fig. 9.—The upper tracings are taken from two quiet areas from bipolar leads over the right and left parietal regions of the head, with delta waves from the monopolar leads to the same regions. The lower record is an example of beta rhythm from the right central region, with a flat line from the left central region.

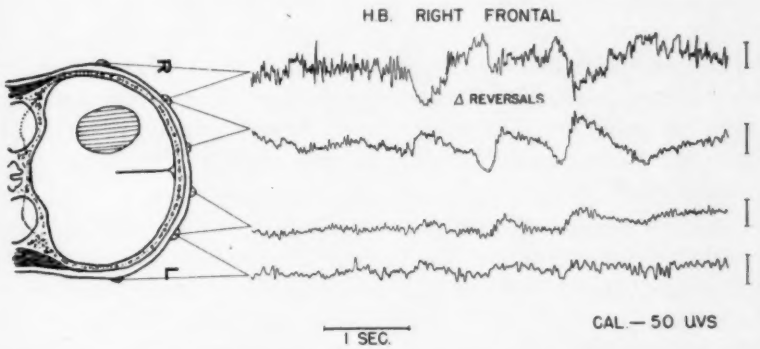


Fig. 10.—Electroencephalogram from a patient with traumatic intracranial hemorrhage. The phase reversals of the delta activity occurred on the cortex lying immediately over the lesion.

fairly deep, rather than a superficial, lesion. The diagnosis of cerebral hemorrhage rather than of some other form of active degenerative lesion cannot be made on the basis of electrographic findings, since the same form of delta activity may be obtained from other intracerebral lesions.

MALINGERING AND HYSTERIA

Since the electroencephalogram is a sensitive indicator of cerebral disorder due to injury to the head and fairly uniform abnormalities are present in all verified cases of damage to cortical tissue, it should be possible to use this method for the diagnosis of malingering or post-traumatic symptoms of a hysterical nature. There were 4 patients in this series whose post-traumatic symptoms were shown later to be due either to malingering or to hysteria. None of these patients showed any significant electroencephalographic indications of cerebral abnormality due to injury to the head. Sample records from the same region of the head of these 4 patients are shown in figure 11.

The first record in this series was taken from patient A. G. shortly after he was cured of "post-traumatic" hemiplegia and hemianesthesia by strong suggestion fortified with electric shocks from a wire brush.

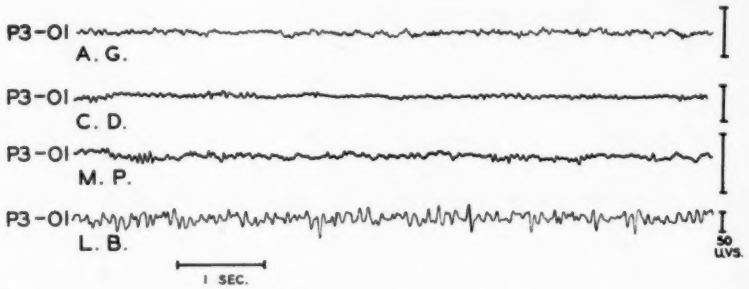


Fig. 11.—Sample records of the electroencephalograms from 4 patients whose post-traumatic symptoms were shown to be due either to malingering or to hysteria.

The patient was terrified at the time of the electrographic examination. Only low amplitude, high frequency potentials were obtained from all regions of the head. The same type of records can be obtained from any normal person as a transient reaction to a startling stimulus or to acute anxiety.[8]

The next two records, from patients C. D. and M. P., also showed the flat, high frequency type of record; both patients had symptoms of acute anxiety and complained of severe headache and "nervousness." The former, C. D., displayed many simulated involuntary tremors and twitches of the limbs throughout the record but only a few movement artefacts, and no corresponding cortical potentials appeared in the electroencephalogram.

8. Berger, H.: Ueber das Elektrenkephalogramm des Menschen, J. f. Psychol. u. Neurol. **40**:160-179, 1930. Jasper, H. H.: Cortical Excitatory State and Synchronism in the Control of Bioelectric Autonomous Rhythms, in Cold Spring Harbor Symposia on Quantitative Biology, Cold Spring Harbor, L. I., New York, The Biological Laboratory, 1936, vol. 4, pp. 320-328; Electrical Signs of Cortical Activity, Psychol. Bull. **34**:456-458, 1937.

The fourth patient, L. B., was uncooperative and combative on admission, following what he reported as an injury to the head with unconsciousness. There were no neurologic signs, and the severity of the injury to the head could not be determined. He was later found to have been psychoneurotic previous to the report of the injury. A fairly normal alpha rhythm was obtained, with only slight irregularities, which were not characteristic of those found due to injury to the head; some resulted from movement artefacts. The electrogram aided in the final diagnosis of psychoneurosis.

There is a clear distinction between the electroencephalograms of patients with cerebral damage as a cause of post-traumatic symptoms and those of patients with a psychologic basis for post-traumatic symptoms and no cerebral injury. In fact, the electrograms of some neurotic patients may be considered opposite in character to those of patients with cerebral injuries. Slow delta waves of large amplitude are present when cerebral damage is present, as contrasted with the rapid waves of small amplitude in certain neurotic and emotional disorders. The importance of this finding for the diagnosis of doubtful cases of "shell shock," war neuroses and "compensation" neuroses is obvious.

COMMENT

Electroencephalographic evidence of abnormal cortical function was obtained from all patients who showed neurologic, mental, serologic or roentgenologic evidence of cerebral trauma following injury to the head. In these cases the degree of abnormality in the electroencephalogram was closely related to the severity of cerebral damage as estimated from clinical examination.

The course of recovery from injuries to the head may be accurately followed by successive examinations showing a progressive return to normal of the electrical activity of the cortex. On the whole, the electrographic signs of improvement were found to parallel closely the clinical signs until the patient approached the normal, when the electroencephalogram appeared to be a more sensitive indicator of abnormality than were other clinical observations. Neurologic and serologic signs of cerebral trauma always disappeared earlier than the delta waves in the electroencephalogram. Careful psychologic examinations would probably show a closer correspondence with electroencephalographic findings, since Conkey[9] has shown that deficiencies in certain performances can be demonstrated long after all apparent physical symptoms have disappeared.

Two patients had complaints of irritability and difficulty in thinking one and two years following a moderately severe injury to the head, with

9. Conkey, H. C.: Psychological Changes Associated with Head Injuries, Arch. Psychol., 1938, no. 232, p. 62.

no other signs of residual damage to the brain. Both showed definite electrographic abnormalities suggesting a neurologic basis for their complaints. Four other patients with more severe complaints shortly after injury had no electrographic signs of cerebral damage and were later shown to have had a neurotic basis for the symptoms. The electroencephalogram should be an important aid, therefore, in estimating the relative importance of neurotic and neurologic factors in a post-traumatic syndrome.

In cases of mild injury to the head the electroencephalogram often provides the only positive indication of cerebral trauma. Fourteen patients showed many delta waves following acute injury to the head, with no serologic, roentgenologic or neurologic signs of cerebral damage. Five of these patients showed some irritability, drowsiness or confusion. Four patients were reported to have been completely normal according to all clinical observations except for the definite abnormalities in the electroencephalogram. In 1 of these cases the abnormalities were atypical for injury to the head, and they did not disappear after recovery from the injury, so that they were assumed to have been present before. The final disappearance of most of the abnormalities in the majority of cases is a clear indication that they were a direct result of cerebral trauma.

Four of the 37 patients admitted because of acute injuries to the head showed normal electroencephalograms. Two of these patients were examined eleven and seventeen days, respectively, after mild injuries, at a time when they were considered clinically normal. The other 2 patients were examined immediately after mild injuries, with no neurologic, serologic or roentgenologic evidence of cerebral trauma. In these cases the electroencephalogram was useful in confirming the absence of damage to cerebral tissue.

The detection of the presence of subdural hematoma or effusion and intracerebral hemorrhage and the possibility of distinguishing between them and generalized contusion or concussion has provided an aid in guiding surgical procedures.

It appears from this study that many of the pathologic changes associated with cerebral trauma, such as edema, petechial hemorrhages and acute swelling of the oligodendroglia, shown by Rand and Courville [10] and others to result from injury to the head, may be reversible if one assumes that the presence of slow delta waves in the electrical activity of the brain indicates such changes. Too little is known of the

10. Rand, C. W., and Courville, C. B.: Histologic Studies of the Brain in Cases of Fatal Injury to the Head: Reaction of Microglia and Oligodendroglia, Arch. Neurol. & Psychiat. **27**:605-642 (March) 1932; Reaction of the Classic Neuroglia, ibid. **27**:1342-1379 (June) 1932; Changes in the Nerve Fibers, ibid. **31**:526-655 (March) 1934; Cytoarchitectonic Alterations, ibid. **36**:1277-1293 (Dec.) 1936.

pathologic basis for slow waves of cortical activity to permit definite conclusions at this time. Whatever its nature, the pathologic processes producing delta waves in cases of acute injury to the head were usually reversible when examinations were carried out over a sufficiently long period. In some cases the delta waves tended to disappear from all regions of the head with the exception of the site of most severe injury (as in the case of focal laceration of the cortex [B. V.] previously mentioned). In such cases the lesion probably provides the material for traumatic epilepsy and other conditions resulting from permanent focal damage. In other cases electroencephalographic abnormalities, such as bursts of slow waves (resembling the activity in what has been referred to as "petit mal" and "psychomotor" epilepsy), persisted but showed no precise localization.

The complete disappearance of delta waves from the site of operative trauma resulting from surgical intervention on the brain (unpublished results obtained in collaboration with Dr. Wilder Penfield), even though they dominated the electrographic picture for several days immediately after the operation, is further evidence that the abnormal condition of the traumatized cortex giving rise to delta waves may be a completely reversible process.

In some cases, however, delta waves, as well as epileptiform waves of various kinds, have been obtained many years after a severe injury to the head. They may persist over a local area or diffusely over most of the surface of the head. If delta waves indicate an active degenerative process, as suggested by Golla, Graham and Walter,[11] progressive degeneration must persist for many years around a severe cortical lesion. Evidence in favor of this assumption is given by the histologic study of biopsy specimens of cortical tissue surrounding old meningocerebral cicatrices, in which Penfield and Humphreys[12] found evidence that active degeneration was taking place.

In the present series of cases there was usually evidence of some generalized disturbance rather than of a purely localized lesion. This may have been due in part to the fact that most of the patients had struck their heads on a large blunt object, such as a paved street. Results might be different, for example, with gunshot or shrapnel wounds.

It is perhaps well to mention finally that delta waves are not always a sign of abnormal cortical activity, since they occur in abundance during normal sleep. It is of some interest to note that the extremely slow random waves found in cases of the most severe cerebral trauma are also

11. Golla, F.; Graham, M. B., and Walter, W. G.: The Electro-Encephalogram in Epilepsy, J. Ment. Sc. **83**:137-155, 1937.

12. Penfield, W. G., and Humphreys, S. P.: Epileptogenic Lesions of the Brain: A Histological Study, Arch. Neurol. & Psychiat. **43**:240-261 (Feb.) 1940.

characteristic of the deeper stages of sleep. When such waves occurred from all regions of the head, with no trace of other types of activity, the patients were comatose. When they appeared only from one area of severe localized trauma there was no significant general impairment of consciousness, but often some irritability or confusion.

It should also be pointed out in this connection that slow cortical waves do not necessarily always indicate cortical injury, since such waves may occur with lesions in the diencephalon.[5a] One patient in this series (A. M.) showed neurologic signs of major damage to the base of the brain and showed the slow random type of delta activity from all regions of the cortex.

SUMMARY AND CONCLUSIONS

Clinical and electroencephalographic studies of 64 cases of cerebral trauma due to injury to the head are presented, in 37 of which the condition was acute. The principal results may be summarized as follows:

1. In cases of acute injury to the head, cerebral trauma was indicated in the electroencephalogram by (*a*) random or regular delta waves varying in frequency from less than 1 to 6 per second; (*b*) poor regulation or disorganization of the alpha rhythm; (*c*) epileptiform discharges.

2. The severity, type and localization of cerebral trauma as judged by the electroencephalogram corresponded closely, in cases of more severe injury, with the results of clinical, roentgenologic and serologic studies and of examination of the spinal fluid, as well as with operative findings. In cases of mild injury the electroencephalogram appeared to be the most sensitive indicator of cerebral injury.

3. The electroencephalogram provides a sensitive objective measure of recovery. Electroencephalographic abnormalities were gradually replaced by normal activity as the patient showed clinical improvement but persisted longer in some cases than did other clinical signs of cerebral disorder.

4. In some of the cases of more severe injury delta and epileptiform waves and disorganized activity were observed in the electroencephalogram several years after the injury. These were associated clinically with changes in personality, epileptic seizures, irritability, disorder in thinking or, in a few cases, with no remarkable clinical abnormality.

5. Post-traumatic syndromes due to malingering or hysteria are clearly evident from the electroencephalographic examination, since in such cases none of the characteristic abnormalities associated with genuine cerebral trauma are obtained.

6. Electroencephalographic indications of subdural hematoma or effusion, epidural hematoma, intracerebral hemorrhage and focal as contrasted with generalized trauma provide an aid to surgical therapy.

ABSTRACT OF DISCUSSION

DR. TRACY J. PUTNAM, New York: This clear presentation shows, I think, the value of routine electroencephalographic examination in everyday clinical work. Electroencephalography provides a new tool, with peculiar advantages and limitations, which serves to supplement and augment other methods of examination of the nervous system and is of enormous importance in the study of a great many problems aside from the cause of convulsions and the localization of tumors, for which its use was first advocated.

While I have not analyzed our own records for the cases of traumatic origin, my impression is that the results which my associates and I have obtained closely approximate those presented by the authors. I believe, however, I should disagree with them on the point that a negative electroencephalogram rules out the possibility of cortical damage. In our experience this has not been the case. It is evidence against the presence of such damage rather than proof of its nonexistence, which is quite a different matter. On the other hand, the presence of abnormal patterns in the electroencephalogram is presumptive evidence in favor of an organic lesion, although this evidence also has to be weighed.

For the sake of clarity, I should like to ask Dr. Kershman to say whether there is anything in the abnormal patterns obtained from foci of cerebral trauma which distinguishes them from the abnormal patterns from other lesions, or whether the pattern depends on the location of the lesion and the cells involved, rather than on the mode of origin of the lesion.

I wish he would also a little more about the difference between the manifestations of lesions deep within the brain and those of the cortex.

I was interested in his tracing the genesis of petit mal complexes as Lennox and Gibbs defined them some years ago, from waves of irregular form and slow periodicity, with final clearing up. I wish he would comment on the presumptive point of origin of these petit mal complexes.

DR. R. S. SCHWAB, Boston: This is an important contribution because it brings to the attention the need of applying the electroencephalographic method to all varieties of cerebral trauma. My associates and I, in our laboratory in Boston, agree with the authors that injuries to the head cause slow waves and that the electroencephalogram is useful in making a prognosis and in estimating the progress of the patient and the possibilities of subsequent local complications.

While it was implied in the paper, I feel that it was not sufficiently emphasized that the changes in the electroencephalogram as followed week by week, or even day by day, are of extreme importance in evaluating injuries to the head. For example, the question arises: "How does one know these slow waves were not there before the patient was struck on the head?" This would be in line with the medicolegal implications which Dr. Kershman mentioned and with which all have had some experience. If one could prove that the electroencephalogram returned to a normal level in a reasonable time after the injury and that after the injury there was steady improvement in the records, one would then have evidence, if the clinical history confirmed it, that the electroencephalogram was presumably normal before the injury. This is one of the most important aids in evaluating the application of the method in cases of injury of the head.

I agree with Dr. Putnam's statement about the diagnosis of hysteria or malingering by this laboratory procedure. All would like to be able to make a diagnosis of hysteria or malingering by a laboratory test which is 100 per cent infallible; I believe, however, that it is impossible and that it is dangerous to assume that a normal electroencephalogram would exclude damage deep in the basal ganglia or the hypothalamus or in the midbrain. Furthermore, the pathologic changes which cause paralysis agitans do not cause abnormal electroencephalograms. We have had cases in which organic changes as gross hemiplegia failed to produce any alterations in the electroencephalogram. It is important to emphasize that this method is simply one more aid in making the diagnosis of hysteria and malingering and that the bulk of the work must be done by careful psychiatric and neurologic examinations.

I should like to ask two questions: Have the authors found any characteristic in the waves in cases of injury to the head which would aid in distinguishing them from slow waves caused by congenital or hereditary epilepsy? Have the authors found resemblance in any of their records to the so-called injury currents reported by Dr. Adrian to occur after experimental injuries in animals?

DR. M. H. WEINBERG, Pittsburgh: This new work has been of great aid, and apparently promises more in the future. However, it seems to me that the paper is a bit dangerous. Clinical neurology, especially, has been recognized as fairly definite and reliable; if, therefore, the authors want to make radical statements, such as have been advanced, they should at least present clinical histories to substantiate them: for instance, in the case of a boy who was said to be unconscious for weeks after the injury, with some neurologic signs, and later was perfectly normal. I, as a clinician for twenty-five years, have yet to see such a case, and I ask Dr. Kershman to give the history in that case.

DR. JOHN KERSHMAN, Montreal, Canada: The time is too short for me to discuss all the points that have been raised, but the material is on exhibit and I shall be glad to consider any individual questions there.

To begin with Dr. Weinberg's question: I have complete histories of all the cases presented, but there was no time to go into detail. I agree with Dr. Weinberg that if a careful psychologic examination had been made on the patient whose chart I showed, abnormalities would have been found; however, although there were neurologic signs on admission these signs disappeared much sooner than the electroencephalographic abnormalities.

So far as the electroencephalographic procedure is concerned, we do not claim it is the method which is going to supersede all others. We do not intend this method to be a substitute for neurologic, roentgenographic or any other form of examination which is now used. We only offer it as furnishing added evidence, which we hope will be of value to the neurologist.

It is true that evidence of a deep injury may not be recorded from scalp leads. However, we have been introducing a lead through the inferior nasal meatus which lies in contact with the mucous membrane of the sphenoid bone. In this way we have at times picked up deep lesions.

With regard to malingering and hysteria, the particular case reported was that of a man who came to the hospital in a state of semiconsciousness. In real states of depressed consciousness, abnormal potentials are always found in the electroencephalogram. Therefore, I think it is fair to assume that if no abnormal potentials are obtained from a patient who is in a semicomatose state, the condition is probably not due to injury of the brain.

As far as the type of the abnormality is concerned, the delta waves are not specific. Exactly the same kind of delta waves occur as the result of an injury to the head as appear with abscess, tumor or any other lesion which may injure cortical cells.

To discuss the origin of epilepsy, especially that of petit mal complexes, would take a long time. However, I believe we have evidence indicating that these rhythmic 3 per second spike and slow waves originate from deep within the brain, rather than from the surface.

The question of return to normal has already been illustrated in 1 or 2 of the cases. If improvement in the electroencephalogram occurs but has not gone so far that the pattern is entirely normal, I think it is fair to assume that there is some residual abnormality.

SUPERSTITIOUS SELF PROTECTION IN PSYCHOPATHOLOGY

G. COLKET CANER, M.D.
BOSTON

Although it is generally conceded that the instinct of self preservation is the most fundamental and most powerful of the instincts, there has to my mind been insufficient emphasis on the part played by self preservation and self protection in psychopathology. It is true that this theme has not been entirely neglected. Alfred Adler and others of his school have emphasized that security is the fixed goal of every person, and that methods of seeking security vary and may result in neurotic symptoms. They have also shown that neurotic symptoms may protect against a feeling of inferiority. Psychoanalysts have stressed the importance of guilt, which infers the importance of self protection, since guilt leads to self protection by expiation. They have also emphasized that anxiety is the central problem of neurosis, but have seemed more interested in the source of the anxiety than in the reaction of self protection to which it leads. It is generally accepted that neurotic symptoms may afford protection by permitting a person to escape with a clear conscience from a responsibility or other situation he cannot face. But it does not seem to me to be generally recognized that superstition makes it possible for neurotic symptoms to have the unconscious purpose of averting threatening situations and of controlling fate. This paper is presented in order to emphasize that symptoms frequently have the unconscious purpose of protecting the subject by controlling fate through a superstitious propitiation of the forces that rule destiny, and also to emphasize the prevalence of superstitions that lead to a state of insecurity and that may, therefore, lead to this superstitious type of self protection.

Two rather conflicting superstitions are of primary importance in causing a state of insecurity. They created fear in the mind of primitive man and may still cause fear today, particularly in a person who is apprehensive by nature. The first superstition is that striking good fortune leads to misfortune, and the second that one misfortune is likely to be followed by others. Although these superstitions are conflicting in nature each was undoubtedly arrived at in the same way. In trying to understand the causes of events, primitive man, probably even more

From the Neurological Service, Massachusetts General Hospital, and the Department of Neurology, Harvard Medical School.

than civilized man, used the *post hoc, ergo propter hoc* type of reasoning. If an event was preceded by any unusual occurrence he picked on that occurrence as the probable cause of the event. Vivid contrasts were impressive and persisted in his memory. A calamity following a period of good fortune was more impressive than one following indifferent fortune. He forgot the latter occasions and remembered the former, and there developed the superstition that unusual good fortune leads to misfortune. The occurrence of a series of misfortunes likewise remained in man's memory, which led to the superstition that misfortunes do not occur singly.

Both these superstitions are also logical results of a belief, widespread in primitive societies and common in civilized society, that any unusual and unexpected event is due to the interference of the gods or spirits.[1] This belief is deeply ingrained in the mind of man and has held its ground throughout the ages, in spite of the growing knowledge of physical and mechanical causes of events. A prayer that danger may be averted from one's self or from a loved person is an indication of this belief, no matter how much one may consciously think and assert that events are governed by natural laws.

The idea was prevalent among primitive peoples that any misfortune may be an indication of unfriendliness on the part of some spirit or god, and in particular that sickness or death, no matter how it occurs, may be the work of some hostile spirit.[2] For instance, in Peru, in the time of the Incas, when a calamity occurred the members of the community were examined until a sinner was found and forced to make reparation to appease the wrath of the god.[3] Even in the Middle Ages it was believed that any disease occurring epidemically was an act of divine retribution, a scourge with which God punished sinful Christians. Man was therefore concerned not to do anything that might antagonize the gods or spirits and was anxious to make expiation and propitiation if there was any indication of their antagonism. It is well known, too, that primitive man, and this is also true of civilized man, had the tendency to think that the gods could be influenced by the same considerations that influenced human beings. They were subject, it was thought, to the same emotions—envy, jealousy, anger, pity and love—and man was egocentric enough to think that his own behavior affected the emotional state of the gods. If he was too fortunate the gods would become jealous,

1. Aldrich, C. R.: Primitive Mind and Modern Civilization, New York, Harcourt, Brace & Company, Inc., 1931.

2. Jevons, F. B.: Introduction to the History of Religion, London, Methuen & Company, 1896, p. 110.

3. Payne, E. J.: History of the New World Called America, New York, Oxford University Press, 1905, vol. 1, p. 443.

a concept that is prominent in Greek literature;[4] hence the superstition that unusual good fortune might be followed by misfortune. If a taboo was broken or a god was otherwise offended, the god might not be satisfied with inflicting one punishment; hence the superstition that misfortunes do not occur singly. Thus, either good fortune or misfortune might be unlucky. These two superstitions would therefore tend to put man constantly on the defensive and would impel him to seek some means of insuring himself against misfortune. It is interesting that the Greek word "deisidaimonia," which came to mean superstition, originally meant fear of the gods.

Examples of the superstition that misfortune follows good fortune are frequently observed in the conversation and behavior of acquaintances and patients.

One often hears: "Why is it that when things are going well something unfortunate always happens?" Recently a patient said: "I have been so happy that it often seems I have a premonition something bad will happen." Another patient remarked: "I am afraid to think that things are better. If I do something always happens." A friend whose child had mastoiditis was told by her husband: "Don't worry; we have always been lucky, and this will come out all right, too." She replied: "That's the trouble. It is because we have always been so lucky that I am afraid this will be the time our luck will change." One hears remarks of this kind so frequently that one cannot doubt that the superstition behind them is present in almost all persons, whether one realizes it consciously or not.

In the recent film version of "The Good Earth" there is a scene in which Wang Lung talks of how fortunate and successful he and his wife have been. His wife, looking up to the sky as though she expected something dreadful to happen, says: "No, no. We have nothing. We are poor humble people; we have nothing." In the book the author stated that "Wang Lung was afraid of his happiness" when he became prosperous and made offerings to the two small gods in the temple who had power over the earth.

In "Stately Timbers," Rupert Hughes, writing about the early Puritans, said: "Matthew was afraid to love his son too well, lest his jealous God send some curse upon them both."

The same superstition is clearly expressed by Schiller in "The Ring of Polycrates," in which are the lines:

"I warn thee still beware of luck
Thy luck is manifest,
Yet tremble for its constancy.
I also have been fortunate.
Each stroke of my despotic state
Has met with heavenly favor kind;
But when I saw my chosen heir
God stricken, I became aware
That fortune leaves a debt behind."

That unusual good fortune is unlucky and that suffering is propitious seem to lie behind various religious formulations, practices and teachings, such as the

4. Herodotus, translated by W. Beloe, Philadelphia, Edward Earle, vol. 2, 1814, p. 167.

idea that those who suffer in this world will be rewarded in the world hereafter and the custom of wearing sackcloth and ashes. In the Bible one finds the following teachings. "He hath put down the mighty from their seats, and exalted them of low degree." [5] "Whosoever shall exalt himself shall be abased; and he that shall humble himself, shall be exalted." [6] "Remember that thou in thy lifetime receivedst thy good things, and . . . Lazarus evil things: but now he is comforted, and thou art tormented." [7] "Blessed are the poor in spirit: for theirs is the kingdom of heaven. Blessed are they that mourn: for they shall be comforted." [8]

These illustrations sufficiently indicate that the ideas have become deeply rooted in the mind of man that good fortune may be dangerous and that suffering is propitious. In his striving to avoid misfortune man will be influenced by these ideas. They will impel him to fear good fortune, to protect himself against its consequences and to cling to some type of suffering as a means of protection.

That suffering may bring increased love, help and protection is learned by almost every one in infancy. The association between a miserable and complaining state, on the one hand, and attention, love, help and protection, on the other, becomes deeply ingrained in each person as the result of his earliest personal experiences. Almost every child learns that in case he has done anything to offend his parents they will be less severe if he appears to be overcome by grief or to be suffering in some other way. He even learns to control his parents by suffering. He may also use this technic later to control or to protect himself against the displeasure of other persons or against that of God; as I have already shown, certain religious teachings tend to encourage this.

Thus one's earliest experiences lead to the development of a mechanism of self protection, through propitiation by suffering. This mechanism may be thought of as all set up in the unconscious and ready to be put into action. When it is set into operation by an appropriate stimulus, it results automatically in sacrifice or in suffering of some type. It may be activated by a threat of any character, particularly if the threat is of such a nature that it cannot be met by conscious purposeful behavior. One may conceive, too, that because this mechanism is unconscious, and therefore dissociated, it may continue to function autonomously once it has been activated. Thus, a neurotic state may be initiated by this mechanism and may continue by its own momentum. I wish to emphasize, however, that a person is rarely conscious of protecting himself in this way, even though his behavior makes it evident. The reaction takes place automatically and seems to be really dissociated from consciousness.

5. Luke 1: 52.
6. Matthew 23: 12.
7. Luke 16: 25.
8. Matthew 5: 3 and 4.

Examples of this type of self protection are not hard to find.

A primitive tribe called the Tongans had the custom of chopping off the end of the little finger as a sacrifice to the gods for the recovery of a sick person.[9]

In "The Ring of Polycrates" this type of self protection is beautifully expressed in the lines:

"Would'st thou immunity from grief?
Then pray the gods in kind relief
To shade thy luck with sorrow's tone;
And if the gods thy prayer deny
Upon a friend's advice rely
And call misfortune to thy side."

Polycrates was persuaded to try to call misfortune to his side and thus propitiate the gods by throwing a very precious ring into the ocean. The following morning a fisherman brought a rare fish to Polycrates, and when the fish was opened the ring was found in its belly. This good fortune was interpreted as a bad omen, indicating that Polycrates was doomed, whereon the royal guest exclaimed:

"With that no longer can I rest,
Thy friendship I no longer own,
The gods 'tis clear thy death design,
I must away or hazard mine."

The Puritans unconsciously protected themselves by this superstitious technic. They felt that things that gave pleasure were offensive to God. They expressed no joy of living but tended to be worried, self persecuted and hypochondriac. Sunday was for them a day set apart for the cultivation of the "good will of God." This they accomplished largely by making themselves as miserable as possible, as though they were paying insurance premiums to forestall calamity by expiation and propitiation.

This same type of superstitious self protection has undoubtedly occurred among all peoples and at all times and is still practiced today. All are familiar with persons who will not let themselves be happy, and who always manage to have some complaint "to shade" their "luck with sorrows' tone."

Pessimism may also be understood in the same way. The pessimist is unconsciously afraid that if he were optimistic unfortunate circumstances would result, so there is developed a compulsion to find something wrong and to protect himself by so doing. It is well understood that pessimism protects a person against disappointment by preparing him for it but not, I think, that it may represent an attempt to control fate by the avoidance of a state that superstition regards as ominous.

Excessive worry may have the same unconscious purpose. An acquaintance recently said that when she is apprehensive she worries and is afraid that what she fears is more likely to happen if she does not worry.

Resistance to getting well, which is usually explained as being due to an unconscious preference for the regressive state afforded by illness, may also be understood as resulting from the superstitious fear of being well. The patient resists getting well because he does not have the courage to face whatever life may bring. He must protect himself against life, and unconsciously reverts to the superstitious technic of self protection.

---

9. Tylor, E. B.: Primitive Culture: Researches into the Development of Mythology, Philosophy, Religion, Language, Art and Custom, ed. 7, New York, Brentano's, 1924, p. 363.

Thus the concept of superstitious self protection reveals an unconscious purpose in certain psychic reactions and symptoms, in some of which such a purpose is not readily seen. It therefore reenforces the validity of one of the most important tenets of dynamic psychology, that of the unconscious purpose in symptoms.

It is not contended that there is no merit in humility, sobriety and similar virtues. It is recognized that there is psychologic truth in statements such as "pride goeth before a fall," and that worry and anxiety may result in a real advantage. When one is overoptimistic or overconfident one is liable not to do one's best. Anxiety and self abasement lead to extra care, greater thought and increased caution, which are real protections. It is, of course, the extra care and thought that count, and not the worry, anxiety or self abasement alone, but it is easy to accentuate and cling to the latter in an unconscious groping for help or protection, because of the association of these with what one is seeking and because they induce a state of misery, which, as a result of early experiences, one unconsciously feels will bring help and protection.

The second superstition of interest here—that misfortunes occur in groups and that if one occurs others are to be feared—is prominent in the minds of savages and is emphasized by students of the primitive mind.

In Hamlet Shakespeare wrote: "When sorrows come, they come not single spies but in battalions." Sayings such as "misfortunes never occur singly" or "it never rains but it pours" are frequently heard.

Examples of this superstition are to be found in the habits of some savages who, if a misfortune occurs, are unwilling to undertake other enterprises on the same day. To them one misfortune is an omen that others are likely to follow.

This same superstition, together with the mechanism of self protection through propitiation, may also be one of the motivating factors in the custom of mourning, particularly in excessive and extravagant mourning. I have already stated that it was not uncommon for primitive man to think that a death, no matter how it occurred, meant the hostility of a spirit or god. Because he identified himself with his clan he felt that a spirit hostile to one member of the clan would be hostile to the whole clan.[10] The inference was that the spirit might not be satisfied with the death of one member; so the death of one member meant that others were threatened and stimulated fear and self protection in them.

Even to those who do not consciously believe that a death indicates the hostility of the gods, such an event is bound to bring home their own vulnerability. This will necessarily stimulate a reaction of self protection, and it seems reasonable to suppose that mourning may at times have in it the element of effecting this by propitiating the gods that control destiny. "In ancient Rome mourners stayed at home and avoided all feasts and amusements, laying aside gold, purple and jewels. They wore black dresses called lugubria or even skins. They cut neither hair nor beard nor lighted fire." [11]

---

10. Jevons, F. B.: Introduction to the History of Religion, London, Methuen & Co., 1896, p. 97.

11. Funeral Rites, in Encyclopaedia Britannica, New York, Encyclopaedia Britannica, Inc., 1910, vol. 11, p. 330.

The well recognized phenomenon that the most extreme mourning may occur when a sense of guilt is present to accentuate fear and the reaction of self protection lends strength to the hypothesis that mourning may at times contain the unconscious purpose of self protection. I do not, however, maintain that this is the sole motivation of mourning. It is obvious that mourning may give expression to real grief, and perhaps to other ideas and purposes.

Physicians see many patients who have become ill after a series of unfortunate incidents, deaths in the family or other threats coming either from the environment or from within the personality. The superstition that misfortunes do not occur singly may be important in such cases, and the symptoms may represent an attempt at self protection through propitiation. In the following cases the symptoms seem to have had this motivation.

REPORT OF CASES

CASE 1.—A woman aged 37 was depressed, wept profusely and had much anxiety. She complained of a choking sensation in the throat and of tightness under the sternum and in the epigastrium and feared she had heart trouble. She felt that she was unable to eat and had lost 10 pounds (4.5 Kg.) in two months. Although she was tired and depressed, it was noted that the anxiety symptoms were more marked than the depression, and a tentative diagnosis of anxiety neurosis was made.

The patient said she had always been apprehensive and described herself as "chicken hearted." She had been the most delicate of nine children and on that account had been given special attention and consideration by her mother. There was no familial history of mental disease, and the patient herself had never previously been in a depressed or hypomanic state.

From her husband it was learned that on an evening two months previously, when the patient was out, the husband, who was at home with his dog, began to think how lonely he would be if the dog died and how terribly lonely he would be if the patient, his wife, died too. He told the patient what he had been thinking when she returned; it disturbed her greatly because she felt it was bad luck to be thinking such things. She said later that she was superstitious and believed that to think things or to mention them might bring them to pass. Two weeks later the dog became sick, and the patient was immediately convinced that her fear would come true and that the dog would die. A week later the dog did die. The patient then became extremely disturbed emotionally and continued in the same condition until she entered the hospital.

In this case the death of the dog suggested strongly that the patient's death was "on the books." The patient reacted with extreme fear. Fear automatically stimulates self protection, and since there was no purposeful way by which the patient could protect herself against this type of threat the instinct had to express itself in unconscious patterns. The excessive overt emotional reaction seemed to represent an attempt to propitiate whatever malevolent influences were at work. In an unconscious groping for protection she seized and clung to the anxiety and other symptoms as a means of gaining the pity and mercy of the Almighty, with the hope thus to erase what seemed to be "on the books."

The patient recovered promptly after explanation and psychotherapy based on this interpretation. A year later she wrote that she had continued to be well and that she felt confident of being able to meet life more courageously in the future.

The patient also showed a superstitious belief in the "omnipotence of thought," in feeling that because her husband had mentioned the dog's death and her death they were likely to happen. Freud [12] has emphasized the importance of this superstition in the affective life of the neurotic person and has stated that the neurotic person is "afraid to express evil wishes lest they be fulfilled in consequence of their utterance." As the superstition applies to thinking as well as to uttering, it seems an important cause of the repression of unacceptable thoughts and wishes. A person would repress unacceptable thoughts because of the fear that if they became conscious they would also become true.

Knowledge of the superstition is of importance in general medicine as well as in psychiatry, since the belief tends to prevent people who have symptoms that they fear may be important from consulting a physician about them. They are afraid that if they act as though something serious were wrong, then it actually will be, and that if they act as though nothing were wrong, then nothing will be. The superstition seems of importance in persons with exaggerated optimism and in the psychology of believers in Christian science. It impels people to try to protect themselves against threats by pretending that they do not exist.

Case 2.—An intelligent woman aged 36 was depressed and easily fatigued, had lost interest in life and was haunted by the fear that she might commit suicide or that something terrible might happen. She disclaimed being superstitious and had never thought of herself as being apprehensive. She had never been depressed before, and there was no history of psychosis in other members of her family. She and her husband had not been getting on well together for about a year. A short time previously a woman friend had been divorced. The patient stated that she felt that she had identified herself with this friend, because they each had marital difficulties. The friend later committed suicide while staying with the patient, and the patient blamed herself for not having looked after her friend more thoroughly. A short time later another woman friend of the patient also committed suicide. She had likewise been divorced a short time previously. The patient remembered thinking: "Is that the fate of us women to be divorced and to have nothing left but suicide?" She became depressed, fatigued and obsessed by the fear of suicide.

In this case, too, there was a strong suggestion that the death of the patient was "on the books," and one way of interpreting the symptoms was that they represented a means of propitiating the con-

12. Freud, S.: Totem and Taboo, translated by A. A. Brill, New York, New Republic, Inc., 1927.

trolling forces of destiny. This patient also improved rapidly after psychotherapy based on this interpretation and reported that she was still well over a year later.

CASE 3.—A business man aged 68 had been well until the latter part of the winter of 1932. He had had no depressions earlier in his life, and there was no history of mental disease in his family except that his mother had been psychotic for two years before she died, at the age of 90. He had been successful in real estate business for thirty-seven years. During this time he had not lost more than $500 in any venture. He had built up a modest fortune. His son stated that making money had always been a fetish with him and that he seemed to have identified himself with his money. He had always been a hard loser. He worshiped success, and to him this meant wealth. He had always been parsimonious.

He denied being superstitious or having any conscious feeling that good fortune was likely to lead to misfortune and vice versa. He remembered, however, that his secretary had said that when things were going well he always seemed to be on his guard. He thought the idea that every rise must be compensated by a fall had been deeply impressed on him by the study of financial charts. When things were going well he would, therefore, feel that they were getting ready for a fall. He said he had always been cautious and that he had always worried a good deal, considering that he had really had little to worry about. He had never been optimistic, but did not think he was pessimistic.

When the financial outlook became bad in 1932 the patient became obsessed by the fact that his real estate holdings had depreciated greatly in value. He became depressed, sleepless and "weepy" and had some difficulty in concentrating. He lost interest in everything, became self centered, felt sorry for himself and had little consideration for others. His condition improved only slightly with the improvement in the general financial picture during the next three years, possibly because the value of the patient's real estate holdings did not improve materially.

In the fall of 1936 the patient's real estate business was even worse. He began to worry more and was soon more depressed, sleepless and given to weeping. He seemed to look for trouble and kept saying that it was inevitable that he and his wife would eventually be on charity, although all the time he knew that they had a good deal of money. It was at this time that the patient came for treatment.

He also improved rapidly after psychotherapy based on the hypothesis that his symptoms were the expression of superstitious self protection. Two years later he reported that he had continued to be well in spite of disturbing financial conditions.

In this case and in case 2 the symptoms were sufficiently characteristic to justify classifying the condition as cyclothymic depression, but the fact that in each case the symptoms had followed experiences which one would expect to induce a reaction of self protection led to treatment based on the presumption that this reaction was of etiologic importance. The rapid improvement with treatment suggested that this presumption was correct, although, of course, such evidence is not conclusive.

COMMENT

Cases in which symptoms follow a threat to the patient either from external situations or from unacceptable urges within his personality are so frequent that one cannot doubt that the fear occasioned by the threat plays some part in the precipitation of the symptoms. The question is: How great is the part and of what type? My thesis is that the fear stimulates self protection and that the symptoms may have the unconscious purpose of obtaining protection through propitiation. The strength of the reaction of self protection and the pattern by which it is expressed are therefore the important factors in the determination of symptoms.

In such cases the patient may complain of somatic symptoms but is more likely to suffer from anxiety and particularly from depression. I do not maintain that all depressive reactions or other states which follow situations causing fear are to be classified as examples of superstitious self protection. It is well known that intense emotion may precipitate epileptic attacks, thyrotoxicosis and other frankly somatic conditions. Many seemingly genuine cyclothymic depressions have their onset following situations causing fear, and although in these cases a reaction of self protection may have been of importance in precipitating the symptoms, I am not prepared to give up the common belief that the primary cause of cyclothymic depressions is some physiologic dysfunction not at present understood. But even if the latter is true, the mechanism of superstitious self protection may be of importance in genuine cyclothymic depressions, because the depression itself may act as an intangible and sinister threat against which the patient is unable to protect himself except by the mechanism of propitiation. It is noteworthy that patients suffering from such a depression can often appear almost normal if a friend or stranger is present. They may be irritated by encouragement and reassurance. They berate themselves, are steeped in pessimism and talk and act as though they had some motive in intensifying their symptoms and in making themselves as miserable as possible. This behavior is appropriate if the unconscious motive is that of gaining the pity and mercy of the powers that control fate.

It is also a matter of clinical experience that even in cases of undoubted cyclothymic depressions, in which the condition at first cannot be influenced by psychotherapy and in which psychotherapy is therefore discontinued, a renewed attack by psychotherapy later in the course of the illness may lead to rapid improvement. If it is true that cyclothymic depressions result from some physiologic dysfunction, the phenomenon just described might be explained by the supposition that the mechanism of self protection by suffering may continue to operate after the physiologic cause of the depression has disappeared. Thus, this mechanism of

superstitious self protection may be of importance even in cases in which some other pathologic factor is present.

I have tried to show that a mechanism of self protection through suffering exists in the unconscious and that it may express itself in pessimism, worry, puritanism, excessive mourning and other neurotic and depressive symptoms. The recognition of the mechanism of superstitious self protection has been of considerable value in treatment. It gives a basis for simple, direct psychotherapy. Realization of the unconscious purpose and advantage of symptoms improves the attitude of the patient toward them. The patient sees that his energies have become absorbed in an orgy of self protection and that he is seeking to achieve this in neurotic and useless patterns. This helps him to redirect his energies toward reality. The physician's way is prepared for an attempt to train the patient to have greater courage and to develop in him a philosophy which will fortify him so that when life "threatens," the response of meeting it will be activated rather than that of self protection. The development of a more courageous attitude in the patient is the major problem in cases of this kind. The patient must learn to meet life rather than to protect himself against it by this superstitious technic.

SUMMARY

Self protection may be stimulated by superstition and may be expressed in superstitious patterns.

The superstition that unusual good fortune leads to misfortune is widespread and leads to a compulsive avoidance of good fortune. This is of importance in puritanism, resistance to getting well, excessive worry and pessimism.

The superstition that misfortunes occur in groups is grounded in the belief of primitive man that misfortunes are caused by hostile gods or spirits. The idea that the powers that control fate may be moved to pity and mercy by suffering is present in the unconscious of most people. It has led to an unconscious mechanism of self protection through suffering. This mechanism may be activated by life threats and by superstition and may continue to function autonomously once it has been activated. It is of importance in the psychopathology of everyday life, in neuroses and perhaps in depressions and other psychoses.

Knowledge of a superstitious belief in the "omnipotence of thought" is of practical importance in psychiatry and in general medicine.

The essential facts are given in 3 cases in which a threat precipitated symptoms which seemed to be the expression of unconscious self protection by suffering.

The development of attitudes which will offset too strong a reaction of unconscious self protection is one of the major tasks of psychotherapy.

PREVENTION OF DISLOCATIONS AND FRACTURES IN METRAZOL CONVULSIONS

J. H. RANKIN, M.D.
WOODVILLE, PA.

The discovery of metrazol (pentamethylethylenetetrazol) convulsive therapy marked an important advance in psychiatry. As with many new forms of treatment, early reports indicated that the method was relatively free of major complications. However, with more experience in the application of convulsive therapy it became evident that serious complications could and did occur. Some reports described complications of so serious a nature and frequency that abandonment of the procedure was recommended by many.

Among those familiar with the results of metrazol therapy there are few who question its value. It is obvious, then, that unless some method for the prevention of complications incidental to its use is developed, one is likely to be deprived of a potent therapeutic weapon. The purpose of this paper is to discuss the anatomic and mechanistic factors which operate to produce fractures and dislocations during metrazol-induced convulsions and to present a technic based on these considerations which has, in my hands, reduced the incidence of complications to such an extent that major complications may be considered rare.

Of ranking importance in metrazol-induced fractures are those of the vertebral bodies. These usually occur as anterior compression fractures of the midthoracic vertebrae. Less serious, but important enough to militate against the use of metrazol are fractures and dislocations of the mandible, humerus and femur. Somers [1] described bilateral fracture of the femoral neck. Bennett [2] described 8 fractures of the dorsal vertebrae in a series of 17 patients treated. Hamsa and Bennett,[3] in a series of "some 800 shocks," found 4 fractures of the femur, 1 of the elbow and 2 of the spine. The vertebral fractures in this series were multiple anterior compression fractures of the vertebral bodies occurring at the level of the sixth and seventh and fifth and sixth thoracic verte-

1. Somers, D. C., and Richardson, R. D.: Bilateral Fracture of the Femoral Necks Caused by Metrazol Convulsions, Am. J. Psychiat. **95**:1193 (March) 1939.

2. Bennett, B. T., and Fitzpatrick, C. P.: Fractures of Spine Complicating Metrazol Therapy, J. A. M. A. **112**:2240 (June 3) 1939.

3. Hamsa, W. R., and Bennett, A. E.: Traumatic Complications of Convulsive Shock Therapy, J. A. M. A. **112**:2244 (June 3) 1939.

brae. Polatin [4] and his co-workers reported the occurrence of 22 fractures of the midthoracic vertebrae in a series of 51 cases. These authors expressed the opinion that many more vertebral fractures would be found if roentgenograms were taken of all patients undergoing treatment. Carp,[5] in an analysis of a series of 687 cases in the New York State Hospitals in which the treatment was given, revealed an incidence of 12 fractures and 118 dislocations following metrazol convulsions. This included 4 fractures of the humerus, 5 of the femur, 1 of the body of a dorsal vertebra, 1 of the transverse process of a dorsal vertebra and 1 of the jaw. Dislocation of the mandible occurred in 102 cases and of the humerus in 16 cases.

MECHANISMS INVOLVED IN FRACTURES AND DISLOCATIONS

Rational preventive technic depends on a knowledge of the anatomy and mechanics of the bones and joints involved, as well as of the nature of the forces of stress and strain operating on these areas during the muscular action taking place in a convulsion. A review of the anatomy and mechanics of function of the mandible and mandibular joint, the upper part of the humerus and the humeral articulation, the upper part of the femur and the coxal articulation and the vertebral bodies and vertebral articulations is considered indispensable to this presentation. This is correlated with an evaluation of the physical forces brought into play at these points during a convulsion.

The Mandible and Mandibular Joint.—The mandibular joint is relatively shallow, but is protected medially and posteriorly by the temporal bone. Anteriorly there is little protection, for the joint must have anterior motion during mastication. Therefore, the most likely direction of dislocation is anteriorly, where protection is least. The muscles involved in this action are the temporalis, masseter and pterygoidis internus and externus, as well as the anterior fibers of the temporalis in their anterocephalad pull. It is at the point of maximum opening of the mouth that dislocation occurs. If none occurs, the jaw closes forcibly at the onset of the second clonic phase as a result of the action of the temporalis and masseter muscles.

Mandibular fractures have been described as secondary to weak bony structures. This may be true in some cases. But when bony structure

4. Polatin, P.; Friedman, M. M.; Harris, M. M., and Howitz, W. A.: Vertebral Fractures Produced by Metrazol Induced Convulsions in the Treatment of Psychiatric Disorders, J. A. M. A. **112**:1684 (April 29) 1939.

5. Carp, L.: Fractures and Dislocations by Muscular Violence Complicating Convulsions Induced by Metrazol for Schizophrenia, Ann. Surg. **110**:107 (July) 1939.

is normal, the powerful upward pull of the masseter muscle, which is inserted at the angle of the jaw, on an immobile, dislocated condyle is more likely to be the specific cause of fracture at the angle of the mandible.

The Humerus and Humeral Articulation.—The shoulder joint is one of the least protected joints in the body. The glenoid cavity is shallow, and the head of the humerus is relatively large. However, in view of the varied functions and large radius of movement of the joint, this architecture is necessary. Consequently protection of the joint depends largely on protection by the muscles. Anteriorly, the muscular attachments of the humerus are the pectoralis major and subscapularis; posteriorly, the attachments are the supraspinatus and infraspinatus, the teres major and minor and the latissimus dorsi; above is the deltoideus. The pectoralis major adducts the humerus and causes inward rotation. If the arm has been raised the pectoralis major tends to bring it downward. The subscapularis rotates the humerus inward and acts in preventing displacement of the head of the humerus. The supraspinatus assists in raising the arm and fixes the head of the humerus in the glenoid cavity. The infraspinatus and the teres minor rotate the humerus outward and carry the arm backward. Thus, the role of the spinati and teres major is one of protection of the shoulder joint. "The teres major assists the latissimus dorsi in drawing the previously raised humerus downward and backward and in rotating it inward." [6]

Fracture through the surgical neck results from a variety of forces. The infraspinatus, teres minor and subscapularis pull the proximal part of the humerus toward the trunk and rotate it outward. This action opposes the powerful adduction of the deltoideus and the inward rotation of the pectoralis major and latissimus dorsi. The arm must be raised for the latissimus dorsi and teres major to exert maximum force downward and backward. Thus, when the arm is raised a marked torsion effect is produced. In addition, the downward pull of the teres major and latissimus dorsi at a point proximal to the insertion of the opposing deltoideus causes maximum force to be exterted on the surgical neck. Fracture through the anatomic neck is caused by the forceful impaction of the head of the humerus in the glenoid cavity.

Dislocation of the humerus anteriorly results from the downward and backward pull of the latissimus dorsi and teres major on the previously raised arm. Posterior dislocation, often associated with fracture, is caused by the same mechanism that produces a fracture of the anatomic neck—forceful impaction of the humerus into the glenoid cavity. It is

6. Gray, H.: Anatomy of the Human Body, ed. 22, Philadelphia, Lea & Febiger, 1936, p. 440.

to be noted that the arm must be in a raised position for these fractures or dislocations to result.

The Femur and Coxal Articulation.—Accidents to the femur, as reported, are apparently limited to the region of the neck and trochanters. Examination of the structure of the hip joint shows the acetabulum to be deep and the capsular ligaments strong. These capsular ligaments, especially the iliofemoral, are important in a consideration of fractures of the neck. The iliofemoral, the strongest ligament in the body, connects the anterior inferior iliac spine with the intertrochanteric line of the femur. Its chief action, other than forming the joint capsule, is to prevent backward tilting of the pelvis. Thus, it plays an important role in keeping the body erect. When the groups of external rotating and abducting muscles (obturator, gemelli, quadratus femoris and glutei) contract mediad and cephalad, the opposing strain is taken by the iliofemoral ligament. Through this mechanism, fractures of the femoral neck occur. In fractures through the trochanters, the group of adductor muscles comes into play (adductor longus, adductor magnus and adductor brevis; pectineus, and gracilis). These muscles, acting from their origin on the pubis and pectineal line to their insertion along the femur, have a powerful adducting action. Thus, the strain of the opposing pulls lies between the trochanters, making this site the most likely point of fracture.

The Vertebral Column.—The forces causing injury to the spine are multiple, since many muscles and groups of muscles are involved in keeping the spine erect. However, since the site of injury following metrazol convulsions apparently is in the midthoracic region, discussion can be limited to the factors involved in anterior compression fractures of the midthoracic region.

Keeping the trunk erect depends on two opposing muscle forces acting on the spinal column. During forceful anteroflexion of the thoracic region of the spine, the spinal erector groups are overpowered by the flexor groups. In reviewing the anatomic characteristics of the spinal erector muscles, it is noted that their mass is least in the thoracic region and greatest in the lumbar and cervical regions. Therefore, of the three divisions of the sacrospinalis muscle, the iliocostalis group has the least extensor power. In addition, the curve of the thoracic vertebrae is anterior, or concave. Thus, any forcible action of the spinal flexor group tends to bend the midthoracic portion of the spine first (fig. 1, diagram *A*). There is also the added thoracic flexing action of the serratus posterior muscles of the erector group. The serratus posterior superior, having its origin between the seventh cervical and the second thoracic vertebra, is inserted into the second, third, fourth and fifth ribs. Owing to the anterior curve of the spine, the fibers of this muscle lie anterior

to the curve of the vertebral column, causing thoracic flexion. The serratus posterior inferior muscle likewise contributes to anteroflexion indirectly by the pull from its insertion on the ninth, tenth, eleventh and twelfth ribs to its origin on the transverse processes of the eleventh thoracic to the third lumbar vertebrae. Thus, one sees that the spinal extensor muscles not only are weak in the thoracic region but also contribute to anteroflexion of the spine (fig. 2).

The anterior muscle groups present a complicated chain of forces that tend to exert great flexor action on the spine, aided by the lever action of the thoracic cage and the individual ribs. In analysis, it is seen that there are several forces acting here. One is a force exerted from the mastoid process of the skull through the sternocleidomastoid muscle

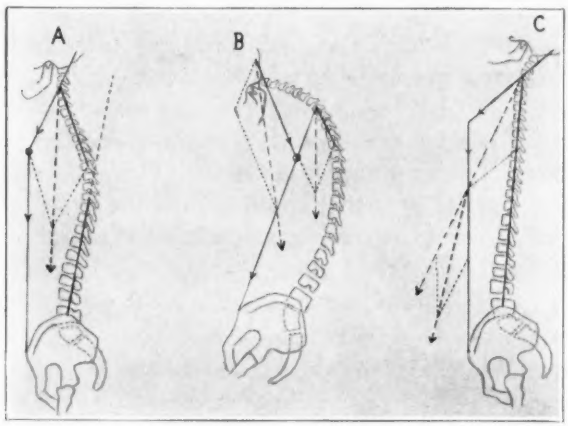


Fig. 1.—Schematic representation of forces acting on the spinal column: *A*, normal spinal contour; *B*, hyperflexion, Polatin method; *C*, hyperextension, advocated position.

to the origin on the sternum when the head is bent backward. The force is transmitted through the sternum to the anterior abdominal muscles, thence to the crest of the ilium, the inguinal ligament and the pubis. This action is aided by the scaleni which help to fix the thoracic cage to the mastoid process, and the serrati, rhomboidei, levator scapulae and pectoralis, which tie the ribs and the upper part of the spine together. Also, because the sternum is far anterior to the spine, marked leverage is available to add greatly to the anteroflexion of the thoracic portion of the spine. Another force is exerted through the humerus and shoulder girdle by the action of the pectoralis and latissimus dorsi in pulling the shoulder down and forward. Each rib is in itself a powerful lever in vertebral movement. A lower muscular system tends to flatten the lumbar curve through action of the obliques internus and

externus abdominis and the quadratus lumborum, which pull the lower ribs nearer the ilium. In this action the diaphragm and the iliopsoas muscle also concur. Thus, in flattening the lumbar curve the normal thoracic curve becomes more angulated and offers greater vulnerability to anteroflexion. This group also tends to flex the thigh on the trunk.

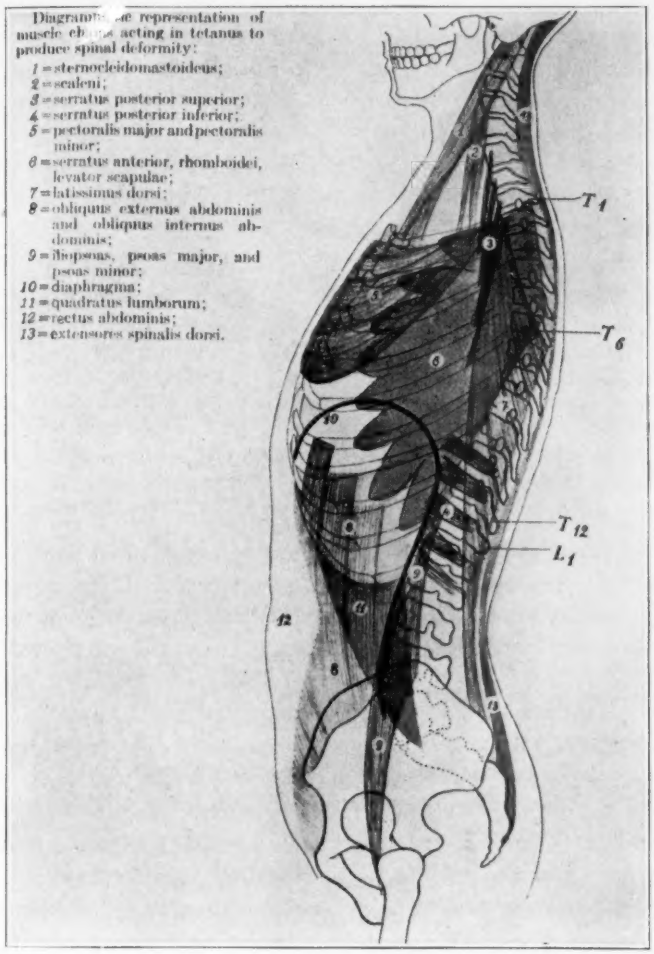

Diagrammatic representation of muscle groups acting in tetanus to produce spinal deformity:
1 = sternocleidomastoideus;
2 = scaleni;
3 = serratus posterior superior;
4 = serratus posterior inferior;
5 = pectoralis major and pectoralis minor;
6 = serratus anterior, rhomboidei, levator scapulae;
7 = latissimus dorsi;
8 = obliquus externus abdominis and obliquus internus abdominis;
9 = iliopsoas, psoas major, and psoas minor;
10 = diaphragma;
11 = quadratus lumborum;
12 = rectus abdominis;
13 = extensores spinalis dorsi.
T1
T6
T12
L1

Fig. 2.—Diagram showing groups of muscles involved in flexion of the vertebral column (Roberg [7]).

Thus, one sees a continuous force acting, with the aid of the thorax as a lever, from the mastoid process to the femur. Anteroflexion of the spine occurs at its weakest point, the midthoracic region.[7]

7. Roberg, O. T.: Spinal Deformity Following Tetanus, J. Bone & Joint Surg. **19**:603 (July) 1937.

PATHOLOGIC CHANGES ASSOCIATED WITH VERTEBRAL FRACTURES

Discussion of the pathologic changes following fractures other than those of the spine can be eliminated because of general familiarity with them. Fractures of the spine, aside from those resulting from external trauma, have been infrequent. Fractures of the spine due to convulsions occurring in tetanus have been reported, but the cases have been few.[7] Since the introduction of the metrazol convulsive treatment the incidence of a similar type of fracture, unfortunately, has risen rapidly. For this reason discussion of the pathologic changes associated with vertebral fractures of this type is indicated. Because of the similarity in means of production and end results, changes in the bones following fractures occurring during tetanus can be described as representative of those occurring during metrazol convulsions.

The mechanical cause of midthoracic fractures, as already discussed, has been stated in Radman's theory of the mechanism of spinal compression, cited by Roberg:[7]

> The force of a jarring or bending fracture of the spine is not transmitted simply in a vertical direction from one body to another, but its horizontal and vertical components are resisted by a third, represented by a sudden tension occurring in muscles fixed at a point anterior to the spine and contracting reflexly. The contraction of these muscles compresses the anterior surfaces of the bodies in a mechanism similar to that of the tetanic curving of the thoracic spine anteriorly.

Traumatic Changes in Bone.—Vertebrae can resist large weights without alteration in shape; but because of the resulting condensation and increased brittleness of the substantia spongiosa, there is decreased resistance to compression and increased plasticity of bone.

> Trip-hammer blows in rhythmic succession reduced the elasticity of the bone after a certain time so that the transient elastic flattening, which at first occurred with each blow, recovered less and less, and the vertebra became brittle and lost its initial resistance to sudden pressure.[7]

Analogous to this is the loss of temper in iron by repeated hammerings.

Immediate Changes.—Shortly after damage to the vertebrae had occurred, microscopic examination revealed, according to Eberstadt, numerous shattered, broken or collapsed trabeculae, comprising a disordered group. Edematous, vascular, fibrillar marrow, containing plasma cells and small round cells with much protoplasm, replaced the medullary cavity. Bäcker, cited by Roberg,[7] described hemorrhages in the intervertebral disk and microscopic "mechanical disorder" of the vertebral body.

Delayed Changes.—Later changes include hemorrhage extending far beyond the line of fracture. This is followed by necrosis and atrophy of bone tissue. There is also hemorrhage in the vertebrae, which show no loss of contour.

> Thus, from physical and pathologic standpoints, where even a slight change has taken place in a vertebral body without alteration in form, the affected bone is more exposed to damage by the normal daily burden. Where a change in shape has already taken place, the weakened link or bent portion throws the entire chain into static decompensation, and a more definite basis is provided for later changes.[7]

It should be noted that recovery may be associated with callus formation, in which case similarity to Kümmell's disease is approached.

DIAGNOSIS OF VERTEBRAL FRACTURES

Since the roentgenogram furnishes the only conclusive evidence of vertebral fractures, some of the criteria for diagnosis are of interest. Fragmentation of the bony structure extending through the periphery of the shadow is certain evidence of fracture. Displacement of one portion of the body against another in a sagittal or frontal direction also demonstrates fracture. Flattening in a vertical direction or an isolated wedge formation associated with a continuous line of increased density in the interior of the body, even in the presence of an intact outline, is suggestive of a break in the substantia spongiosa. The formation of a sharp angle at the junction of two lines which are drawn through the longitudinal axes of successive vertebral bodies in a lateral view of the spine is suggestive of fracture. This, however, can apply only to a sharp break in the contour.

Consideration must be given to the possibility that in some cases metrazol-induced fractures may not be true traumatic fractures, but may be due in part to conditions associated with the youth of the patient. Thus, in considering any fracture after administration of metrazol, the age of the patient and the past medical history are important. Roberg [7] gained "the impression that the adult spine is more resistant to tetanus and less plastic than the adolescent spine." Also, if regressive changes do take place in adults, they are not accompanied by the same changes in the end plate region as are seen in the incompletely developed vertebral column of the adolescent.

An aid in the differential diagnosis of juvenile kyphosis and fracture is found in the site of fracture. In post-tetanic (or metrazol induced) fracture the break occurs at the level of the fifth and sixth thoracic vertebrae. In the juvenile type of kyphosis the changes occur usually at the level of the ninth thoracic vertebra.[7]

In general, it is seen that spinal fractures are more prone to occur in adolescents. The site of post-tetanic fracture is higher than in juvenile kyphosis.

SUGGESTED METHODS FOR PREVENTION OF VERTEBRAL FRACTURES

Prophylactic measures are at present uncertain, varied and admittedly in an experimental stage. Polatin [4] offered a method of posture by

which the patient's spine is acutely anteflexed during the convulsion. Bennett [2] expressed the belief that the use of a modified Bradford frame, with mechanical restraint, may be the answer. Hamsa and Bennett [3] have controlled the severe flexing action of the muscles by spinal anesthesia, using 10 mg. of pontocaine hydrochloride N.N.R. dissolved in 4 cc. of spinal fluid. This is injected into the spinal canal between the first and the second lumbar vertebra from thirty to sixty minutes before the administration of the metrazol.

The anesthesia is brief and controls the violent muscular spasm by nerve blockage. This is believed by some authorities to be the solution of the problem of vertebral fractures.[8] The question of the advisability of using restraint during the convulsion was mentioned by Carp.[5] He stated:

> Forceful manual restraint or the use of restraining sheets should be minimized. Clearly, an additional counterforce added to an already existing pathologic force has a tendency to increase spasm and this causes a greater likelihood of injury.

COMMENT

In devising a method of minimizing spinal trauma, particularly in the vulnerable thoracic region, several factors must be taken into consideration. The strength of muscle pull must be considered. Although it is impossible to measure the exerted tension in most cases, it is known in general that the amount of work done depends on the formula: muscle mass times length of contraction. The position of the joint with the amount of leverage exerted on it is also a factor. The question arises whether the muscles, which in contracting cause the damage, should be shortened to their minimal length, thus causing less work to be accomplished. This undoubtedly would decrease the force exerted on the vertebrae. Generalized flexion of the trunk and legs, as advocated by Polatin, would lessen the length of pull, thus decreasing the force exerted on the spine. Also, the leverage exerted by the action of the ribs would be decreased. The effect on the spinal extensor muscles would be to increase their contractile distance, thus increasing their efficiency in opposing the flexors. The Polatin maneuver also would tend to cause a distribution of flexor force over a greater vertebral area, relieving concentrated stress on a few midthoracic vertebrae. However, in a general flexion of the spine the distance between bodies of the vertebrae is decreased. Thus, when the muscular contraction occurs the anterior portions of the vertebral bodies have to travel a shorter distance to exert force on one another. Also, in spite of the shortening of this contractile distance of the flexor muscles, it must be remembered that a cut muscle

8. Fracture of the Spine During Metrazol Therapy for Dementia Praecox, editorial, J. A. M. A. **112**:2292 (June 3) 1939.

will retract a much greater distance than its maximum when attached to the points of origin and insertion. In other words, in spite of all possible shortening the muscle is still capable of marked contraction. In the intensity of a metrazol convulsion the muscles will contract to such an extent that the spine will become even more flexed, especially in its upper portion, because of weakness of the opposing muscles. In diagram *B* of figure 1 it may be seen that the flexor force acts on the upper part of the spine at two main points, the mastoid process through the sternocleidomastoid and scalenus muscles and the first thoracic vertebra through the first rib. The resultant of these forces tends to flex first the cervical on the thoracic portion of the spine, then, in turn, the thoracic on the lumbar portion. When the weakness of the thoracic extensor muscles is kept in mind, it is apparent that angulation will still tend to occur chiefly in the region of the midthoracic vertebrae, even though there is diffusion of compression throughout the spine. It is also difficult in actual practice to keep the thighs flexed on the trunk, owing to the contraction of the powerful gluteal muscles, which cause extension of the thighs on the trunk. Possible subclinical diffuse damage to the vertebral bodies and changes in the intervertebral disks, in addition to recognized changes, must be considered and are more likely to occur under these circumstances.

The better position for prevention of spinal fractures is one of extension. Bennett advocated this in his use of a modified Bradford frame. If this position is obtained, the contractile distance of the anterior flexing muscles is increased rather than decreased, thus increasing the potential contracting force. Conversely, the contractile distance of the spinal erector muscles is lessened, thus weakening their efficiency as a counterforce. Although this apparently is defeating the purpose of fracture prevention, it actually is not, for with the spine in extension the resultant of forces almost parallels the axis of the spine (fig. 1, diagram *C*). In spinal flexion the resultant of forces is at an acute angle with the spine. In extension the forces tend to be vertically compressive throughout the vertebral column. The anterior portion of the distance between the intervertebral disks is also widened. In flexion the compressive force tends to focus on the anterior portions of the vertebral bodies and the anterior margins of the intervertebral disks. In extension the compressive force tends to diffuse evenly throughout the disks. Extension of the thighs on the trunk tends to tilt the pelvis downward and increases the lumbar curve. This causes the lumbar region to be the fulcrum of the "vertebral lever" rather than a point higher in the spine, which is a more vulnerable area.

Repeated spinal anesthesia, as advocated by Hamsa, does not seem practicable. The usual routine of metrazol treatment is to produce

convulsions three times a week. A total of from five to twenty convulsions is considered a course of treatment, depending on the progress of the patient. It should also be remembered that all injections of metrazol do not necessarily cause convulsions. If spinal anesthesia is necessary as a routine preventive, it obviously precludes any widespread use of metrazol. Certainly, administrators of many publicly supported hospitals would hesitate to institute such routine anesthesia because of the time element, technical difficulties and expense. There is one factor favorable to this measure: the undoubted prevention of clinical fractures and of subclinical damage to vertebrae which might become "clinical" later. However, as a general technic applicable to use in most hospitals, it is hardly practical.

An answer to the use of manual restraint, as advocated by Carp,[5] is contained in the statistics of his paper. In New York State there was only one hospital, the Hudson River State Hospital, that used manual restraint. Among 16 patients there was only 1 dislocation of the shoulder. Dislocation of the mandible occurred in every instance. These figures contrast favorably with those from other hospitals not using restraint. It is almost inconceivable that from manual restraint there could be any additional spasm of a muscle undergoing the contractions of a metrazol convulsion. Instead, it would be expected that the muscle would rupture at some point rather than increase in intensity of contraction. Also, the factor of lever action must be considered. If the leverage exerted on the most likely point of injury is decreased, the exerting force is consequently lessened also. Thus, if manual restraint will favor decreased leverage for the muscle to act against, there should be less chance of injury. This means that there is some one position of the part of the body in question that favors lessened leverage and, consequently, lessened chance of fracture.

ADVOCATED TECHNIC

The Mandible.—During the first year of treatment with metrazol mandibular dislocations were so frequent as to be routine, and so no tally was kept after a few months. Also, reduction was so easy during the relaxed postconvulsive period that this dislocation was not considered a major complication. Gradually new methods have been evolved, however, so that dislocation of the mandible now is rare if the proper technic is used.

At the time of initiation of the convulsion an assistant stands at the patient's head, facing the feet. The palms are placed on the temporal regions of the patient's head. The thumbs are bent and forcibly pressed into the cheeks under the zygomas. This puts pressure directly on the coronoid processes of the mandible, preventing excess forward movement

of the joint by the pull of the pterygoid muscles. Simultaneously another assistant supports the jaw by upward pressure when the "yawning" stage appears. This assistant's other hand is used to free the lips from the teeth and insert a flexible, padded gag for prevention of biting the tongue. Once the mouth closes, upward pressure is continued to prevent "champing" on the gag, with its attendant danger of biting the tongue or lips. The attendant holding the head and pressing on the coronoid processes is also useful in controlling general bodily movements by "anchoring" the patient's head to the bed.

The Humerus.—The cardinal point to be remembered in preventing injury to the humerus is that the arm must be raised for maximum strain on the bone to be effected by the groups of antagonistic muscles. By holding the arms at the patient's sides during a convulsion, fractures and dislocations can be prevented. This is best accomplsihed by holding the wrists, thus keeping the arms in extension and adduction. This procedure also prevents internal rotation. Added protection is offered by having another assistant pin the shoulders to the bed by pressing downward on them. This decreases scapular movements and torsion of the trunk.

The Femur.—In studying the directions of stress on the femoral neck and trochanters, it is to be noted that there is no feasible method of changing either the angles of the bone through which stress occurs or the distance through which the muscles work. Nevertheless, there are two factors which might help to decrease the forces tending to fracture. The first takes into consideration the fact that there is a tendency to powerful external rotation of the femur by the groups of muscles acting in the machanism of fracture. These are the piriformis, obturator internus, gemelli and quadratus femoris. The external rotation of these muscles ceases when the thigh is flexed on the trunk, and they abduct only.[9] In addition, the psoas major, an external rotator muscle, is relaxed because of the flexion of the thigh. Thus, with the femur flexed on the trunk, the tendency toward outward rotation would be lessened and the fulcrum of the lever would be transferred from the femoral neck to the acetabulum, where the ball and socket joint enables the movements to be accomplished with a minimum of strain. However, in actual practice, during a convulsion it is difficult to control the patient with the thighs flexed on the trunk and the legs flexed on the thighs. This position does tend to tilt the pelvis upward, lessening the pull of the anteroflexor muscles. On the other hand, the pull of the heavy iliolumbar and massive gluteal muscles often lifts the patient off the bed into opisthotonos. In this position the strain is transmitted to the

9. Gray, H.: Anatomy of the Human Body, ed. 22, Philadelphia, Lea & Febiger, 1936, p. 477.

upper thoracic and cervical vertebrae, causing angulation and defeating the purpose of minimizing strain on this area. In my experience it has been found that greater control over the patient during a convulsion is afforded by keeping the lower extremities extended and adducted. By this means the groups of smaller abductor and external rotator muscles have unfavorable leverage, because of their origins on the ilium and sacrum and their insertions on the great trochanters. Unusual movements of the trunk to the side, as well as rotations and extensions, are reduced to a minimum also. This control is obtained simply by having an assistant sit on the patient's thighs.

The Spine.—Because of the widening of the anterior portion of the intervertebral spaces, the changing of the resultant of forces to one of vertical compression and better control over the patient, extension

Fig. 3.—Photograph illustrating technic of controlling fractures and dislocations. Note hands in axillas, thumbs under clavicle and control of jaw and head. Most of the attendants are on one side of the bed for photographic purposes.

of the thoracic portion of the spine is the position of choice for metrazol treatment. With this in view, a small hard pillow, 8 by 12 inches (20 by 30.5 cm.), is utilized. In thickness it varies from ½ to 4 inches (1.3 to 10 cm.) on a double tapering scale, with the maximum thickness about 3 inches (7.6 cm.) from one end. The pillow is placed under the patient's back, with the maximum thickness opposite the fifth thoracic vertebra. At the time of onset of the convulsion an assistant forcibly pins the shoulders down by placing a hand on the pectoral muscles, with the fingers in the axillas and the thumbs in the supraclavicular fossae. This maneuver decreases the tendency to anteroflexion and tends to maintain thoracic extension. Lateral rotation of the spine is also prevented. Considerable aid in this is given by the assistants who by holding the head and protecting the mandible prevent flexion and rota-

tion of the cervical vertebrae, thus making the resultant of forces approach a parallel with the spinal axis. The lumbar portion of the spine is anchored in extension by a fourth assistant sitting astride the patient's thighs. This procedure prevents flexion of the thighs on the trunk, and there is a consequent tendency to lumbar anteroflexion. This anteroflexion tends, in general, to help extend the thoracic portion of the spine. In actual practice the patient is seen to bend and extend at the lumbar region during the convulsion, rather than at the thoracic region. The fourth assistant also holds the patient's wrists to prevent damage to the humerus (fig. 3).

RESULTS

This technic is the result not of a brief survey but of progressive accumulation of preventive measures over a period of two years. Various methods were tested; some were discarded, some perfected. Obviously, the technic for the protection of the vertebrae is newest. Previous to elaboration of the technic described here there were occurrences of vertebral fractures. Unfortunately, the exact number is unknown because roentgenograms were not taken of the spine after treatment in all cases. The last 18 consecutive patients completing treatment were managed with the technic described here. Roentgenograms of these 18 patients after completion of treatment showed no evidence of vertebral fracture. By this I do not claim that subclinical trauma has been eliminated. Only the future health of these patients will demonstrate that. However, I know that gross fractures have not appeared in this series of cases. Since repeated trauma may cause decreased resistance, it is advisable that a minimum number of convulsions be produced in each patient. If a patient is showing little improvement after eight or ten convulsions, the chance of improvement with a greater number is slight. I recommend that treatment be not unnecessarily prolonged.

As already stated, mandibular dislocations have become rare. When they do occur they can be traced directly to inexperience of the assistant or to carelessness, if the technic outlined is employed. In over 3,000 major convulsions which have been induced, I have seen no fracture of the mandible.

There has been 1 fracture of the neck of the humerus; no fractures of the femur have been observed.

In view of the rarity of mechanical complications, I am committed to the use of manual restraint, intelligently used, in convulsive therapy.

SUMMARY

Metrazol therapy has been threatened with abandonment because of fractures and dislocations which have been caused by the convulsions.

These have consisted of injuries to the mandible, humerus, femur and thoracic vertebrae.

Prevention of these complications depends on knowledge of the anatomic mechanisms involved in their production. These are described. The preventive methods of other workers are discussed.

A technic to prevent mandibular dislocation and fractures of the humerus and femur is described. Vertebral injury is prevented by a method of spinal hyperextension.

By proper manual restraint, fractures and dislocations due to metrazol convulsions may be prevented.

RELATION OF AGE TO MOTOR IMPAIRMENT IN MAN AND IN SUBHUMAN PRIMATES

MARGARET A. KENNARD, M.D.
NEW HAVEN, CONN.

INTRODUCTION

The earliest motor activity of the normal infant of any vertebrate form is relatively simple and stereotyped in pattern. Later, with the functional and anatomic development of the motor cortex, increased complexity of skilled and coordinated movement appears. This is particularly evident in primates—monkeys, chimpanzees and man—since prehensile finger movements occur in these forms. The paralysis which follows destruction of the motor cortex in man may appear as a "cerebral palsy" after birth injury, or as a hemiparesis in the adult. In all primate forms destruction of a specific motor region is followed by a specific and predictable motor deficit, but the present study indicates that the age of the individual directly affects the deficit in subhuman primates and in man, since removal of a known cortical area from the infant causes a paralysis of different quality from that which occurs after a similar cortical ablation in an adult of the same species.

Definition of Terms.—Much confusion exists concerning the definition of paralysis, spasticity and flaccidity, since each term is used, both clinically and in experimental physiology, to describe a wide variety of signs and symptoms accompanying disorders of the motor system. The paralysis which follows complete transection of the spinal cord has characteristics different from those caused by a lesion of the internal capsule; yet each may be spastic or flaccid, and the degree of each quality may vary in individual instances with recovery, or even with moment to moment changes in the condition of the subject. Spasticity, in particular, is influenced by such factors as fatigue, emotional status and degree of muscular relaxation. Paralysis may be "complete" or "slight" (the term paresis is usually applied to the latter state).

The motor deficit which follows cortical destruction was described thus by Hines:[1] "In man, ablation of, or injury to, the motor cortex and its projection

---

From the Laboratory of Physiology, Yale University School of Medicine.

This work was aided by a grant from the Friedsam Foundation, Child Neurology Research.

The chimpanzees used in this study were acquired as a loan from the Laboratory of Primate Biology of the Yale University School of Medicine and had been born in the Primate Station of that institution at Orange Park, Fla.

The work on human infants was carried out at the Children's Hospital, Boston, through the cooperation of Dr. Bronson Crothers during the summer of 1936, at which time the author held a fellowship from the Rockefeller Foundation.

1. Hines, M.: The "Motor" Cortex, Bull. Johns Hopkins Hosp. **60**:313-336 (May) 1937.

pathways presents two diverse elements, paralysis and spasticity. The paralysis is selective, choosing, for impairment or loss of voluntary movement, all skilled and isolated movements of the hand and fingers, extension of the proximal joints of the arm and flexion of those of the leg. The spasticity (Walshe, 1929) includes three phenomena which resemble somewhat in quality but not in distribution those which characterize the phenomena of release in decerebrate rigidity. These three phenomena of release are muscular hypertonus, clonus and brisk tendon reflexes."

In my experience, in spite of variability, the characteristics of the paralysis and spasticity which appear after cortical lesions are consistent and coincide with those described by Hines. For the purposes of this paper, therefore, paralysis of cortical origin, or paresis, meaning a lesser degree of motor deficit of the same type, has the attributes just described, namely: selective impairment or loss of voluntary skilled and isolated movements of the hand and fingers, of extension of proximal joints of the arms and of flexion of the legs. Spasticity of cortical origin, if pronounced, exhibits muscular hypertonus, clonus and brisk tendon reflexes, as described by Hines.[1] But, as will be shown later, the first signs of spasticity in the monkey are increased resistance to passive manipulation and increase of the tendon reflexes. Clonus may never appear if the spasticity is only moderate.

The quality of the increased resistance to passive manipulation is difficult to describe, largely because it is subject to variations and influenced by emotions, voluntary movements and fatigue. Nonetheless, it can be recognized and distinguished from other types produced by lesions elsewhere. This spasticity is characterized by increased resistance to passive manipulation which, in terms of the clinicians, is of the "clasp knife" variety; that is, resistance to passive movement is greatest at the beginning, but later, with extreme flexion or extension resistance, suddenly disappears and the limb "gives." "Lead pipe" resistance of a plastic type is never found.

In the data to be presented the relation of the age at which cortical injury is sustained to the quality of motor deficit, with particular reference to the two qualities paresis and spasticity, is reported for three primate forms: man, the chimpanzee and the monkey. The influence of the cerebral cortex on motor activity is greatest in man; so in the absence of the motor cortex the deficit is greatest in the human being. Motor activity in the monkey is much less gravely affected by cortical ablations, and the chimpanzee, lying between the two in the evolution of cortical dominance, presents an intermediate type of behavior, which, however, resembles more nearly that of man than of the monkey, both under normal conditions and after destruction of the cortical motor areas.[2]

EXPERIMENTAL DATA ON MONKEYS AND CHIMPANZEES

During the past few years a number of monkeys (baboons [Papio papio] and monkeys [Macaca mulatta]) and chimpanzees have had cerebral ablations performed in infancy, and the subsequent development

2. Fulton, J. F., and Keller, A. D.: The Sign of Babinski: A Study of the Evolution of Cortical Dominance in Primates, Springfield, Ill., Charles C. Thomas, Publisher, 1932.

of these animals has been watched over a period of years. The oldest monkey of this series is now 6 years of age, and a number of others are nearly mature, at the age of 2 or 3 years, which in the life span of the monkey is equivalent to 10 years or more in the life of man. Two chimpanzees have been observed under the same conditions. Early observations on many of these animals have been reported elsewhere.[3] A study of their subsequent growth and development has brought to light many interesting factors related to paresis and spasticity. Motor deficits have in every instance been compared with those which appear after similar operations on adult monkeys and chimpanzees.

Fig. 1.—Posture of 3 normal infant monkeys (Macaca mulatta) at the ages of (*A*) 4 days (infant 41), (*B*) 14 days (infant 36) and (*C*) 18 days (infant 35). Note reflex grasping and improvement in coordination in the older animal.

MOTOR DEFICIT IN INFANT MONKEYS

Normal Motor Activity at the Age of 3 Weeks.—The motor performance of a normal 3 week old infant monkey, Macaca mulatta, is stereotyped, and there is little indication of discrete skilled movement. Such infants can right themselves, stand and move in rhythmic progress, which is of a slow and unsteady type, and on a broad base. They climb

3. Kennard, M. A.: Age and Other Factors in Motor Recovery from Precentral Lesions in Monkeys, Am. J. Physiol. **115**:138-146 (March) 1936; Recovery of Function in Infant Monkeys Following Cortical Ablations, ibid. **123**:118 (July) 1938.

adeptly and tend to cling whenever possible (fig. 1). Volitional prehension is absent, but reflex grasping is strong and sucking is a predominant feature. Motor activity is similar in many respects to that of the "thalamic" adult monkey deprived of the motor and premotor cortex of both hemispheres (areas 4 and 6, fig. 2), in which reflex grasping and righting movements predominate.

Unilateral Ablation.—The effects of unilateral ablation of cortical motor areas in infancy has been described more fully elsewhere.[4] In individual monkeys area 4 (1 animal), areas 4 and 6 (4 animals, fig. 2), the entire frontal lobe (5 animals) and one hemisphere (3 animals) were removed during the fourth week of life, at a time when motor performance was highly stereotyped. The immediate resultant motor deficit after each type of ablation was far less than that which followed a similar ablation in an adult animal, doubtless because intricate motor performance had not yet developed. The paresis was minimal; the

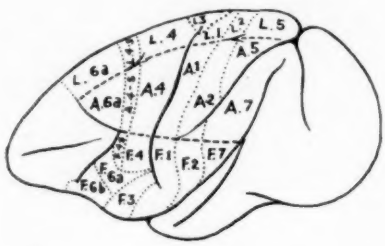


Fig. 2.—Map of sensory areas of the monkey's cortex (Macaca mulatta) (after Dusser de Barenne, J. G.; McCulloch, W. S., and Ogawa, T.: J. Neurophysiol. **1**:436-441, 1938).

infants, on the day after operation, were able to right themselves and cling as before by reflex grasping in all four extremities. There were slight transient eversion and extension of the affected right extremity, but there was no increase of resistance to passive manipulation or alteration in the character of motor performance. Tendon reflexes at the elbow and knee were not increased, and there were no abnormal finger and toe jerks such as appear in the adult after a similar ablation.

A normal infant monkey begins to acquire "voluntary" prehension during the second month of life. The hands are used at first for steadying food objects lying on the floor, later for picking them up. The fingers then begin to be used individually to investigate objects, because of the natural curiosity of the animal. The grasp reflex and

4. Kennard, M. A.: Reorganization of Motor Function in the Cerebral Cortex of Monkeys Deprived of Motor and Premotor Areas in Infancy, J. Neurophysiol. **1**:477-496 (Nov.) 1938; footnote 3.

the tendency to cling become less. If motor regions have been removed previously from one hemisphere the normal extremities begin to show the advanced type of movements before the affected extremities. There is then a noticeable preference for the normal hand in all fine movements. Forced grasping disappears earlier in normal than in abnormal extremities, but there is no increase at this time in resistance to passive manipulation, and knee jerks remain equal. Four such animals (1 a hemidecorticate monkey, no. 11; 1 with frontal lobectomy, no. 19; and 2 with ablations of motor areas nos. 7 and 23) have been kept more than two years. During the first year no increase in resistance to passive manipulation appeared in any instance. During the second year the hemidecorticate animal began to show increased resistance to passive manipulation, which was slight but definite. For comparison, 3 older animals (weighing between 2 and 3 Kg. and probably in the second or third year of life) have each had one hemisphere removed. Each has maintained a definite moderate increase in resistance to passive manipulation in the extremities contralateral to the ablation, which appeared during the first weeks after operation and has persisted for ten months; each has increased knee jerks and marked permanent paralysis of fine distal movements.

Thus, unilateral removal of the motor areas (areas 4, and 4 and 6, the frontal lobe or the hemisphere) in infancy, during the period before complex "voluntary" motor activity appears, is followed by much greater development of motor power and coordination than follows similar ablations in adult life. The immediate effects of operation are slight, but with the appearance of fine motor coordination in the normal fingers, paresis of mild degree becomes obvious in the extremities opposite the lesion, although no spasticity appears at this time. Such paresis is manifest as inability to perform fine purposeful prehensile movements of the distal portions of the extremities, or as failure to acquire or learn these coordinate movements in the normal manner.

Seriatim Ablation of Areas 4 and 6 from Both Hemispheres.—Ablation of the second areas 4 and 6 made at a later age (5 animals) indicates that bilaterality of function is much greater in the motor field if the first areas 4 and 6 have been removed in infancy than if they are extirpated in adult life. For when, after removal of areas 4 and 6 of one side during the fourth week of life, cortical extirpation is made of areas 4 and 6 on the other side at the age of 6 months or more, motor deficit increases bilaterally. There follows some bilateral impairment of discrete skilled movements of the fingers. Such an animal (infant 1) was able to feed itself by use of either hand, but individual finger movements in each hand were less accurate than before the second

operation; the hands and feet became everted; the fingers and toes were spread. There was also an increased tendency to cling and suck, a return to the early patterns of behavior. There was no increase in resistance to passive manipulation for some months after the second operation; then gradually a slight increase in resistance appeared; the extremities became more extended and the use of the fingers more restricted.

It will be remembered that similar bilateral ablations of areas 4 and 6 in the adult caused virtually complete cessation of volitional movements.[5] Spasticity in such adult preparations appears almost immediately after operation and is extreme, but subject to change with change in posture.

Ablation of Other Cytoarchitectural Fields.—Removal of other cortical areas from the infant also affects motor performance,[4] since when areas 4 and 6 and the postcentral gyrus (areas 3-1-2) were removed bilaterally from 1 infant (no. 4), the left at 3 weeks and the right at 6 months of age, a motor deficit appeared which was somewhat greater than that which followed seriatim ablation of areas 4 and 6 alone. Spasticity could be first demonstrated during the fourth week after the second operation. Ultimately it became more extreme in this preparation than after removal of any other areas from other infants. Motor paresis was also greater than that which followed bilateral ablation of areas 4 and 6 only. This animal, still alive, is able to walk, run and climb; it uses the hands for feeding purposes, but poorly. Its motor deficit is great.

The frontal association fields (areas 9-10-11-12) together with area 8 also influence motor performance in the animals operated on in infancy, for their removal after areas 4 and 6 have been ablated bilaterally will add to motor paresis and to spasticity. No such effect is produced in older animals, in which the frontal association areas and the postcentral gyrus have been found to have little effect on motor performance.[4]

Bilateral seriatim ablation thus demonstrates that the cortex has a lesser degree of specificity in the young monkey than in the adult with respect to integration of motor performance. However, if enough cortical tissue has been removed in infancy, skilled motor acts are less well executed as the animal develops. Spasticity appears much later than paresis, if at all, and is never more than slight.

Simultaneous Bilateral Ablation of Areas 4 and 6.—Simultaneous bilateral ablation of areas 4 and 6 before complex "volitional" motor

5. Bieber, I., and Fulton, J. F.: The Relation of the Cerebral Cortex to the Grasp Reflex and to the Postural and Righting Reflexes, Arch. Neurol. & Psychiat. **39**:433-454 (March) 1938.

performance appears has a more marked effect on later development of skilled movements than has seriatim removal of identical regions. An immediate effect on the early type of motor performance is also detectable. In 3 infants (2 macaques, nos. 35 and 36; 1 baboon, no. 22) areas 4 and 6 were removed from both sides at one operation and before voluntary prehension had appeared. These operations were performed with the animal under ether anesthesia, as were all operations on the infants, so that it was possible to observe motor performance within an hour after the close of the operation. Immediately thereafter these infants were able to right themselves, stand and progress rhythmically,

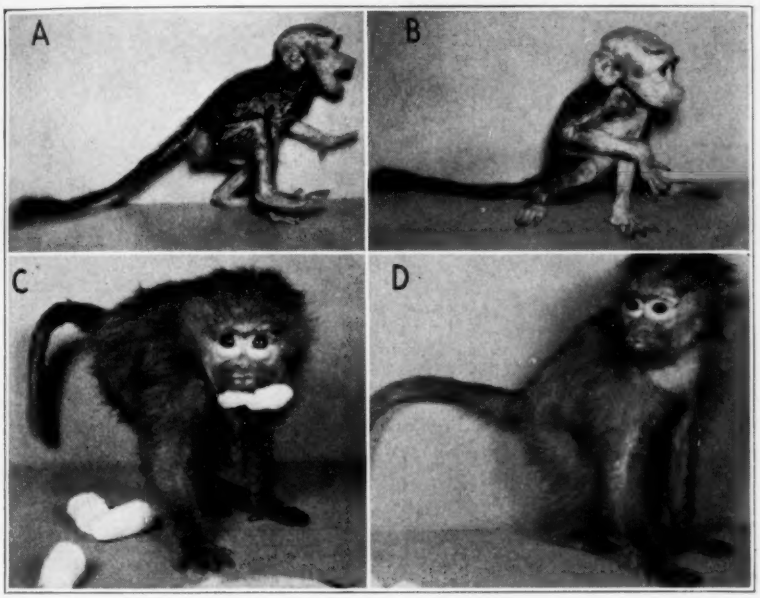


Fig. 3.—Infant baboon 22, from which areas 4 and 6 were ablated bilaterally at the age of 55 days. Postures *A* and *B* were photographed seventeen days after operation; postures *C* and *D* which are nearly normal, six months after operation. Compare with figure 4.

but far less adequately than before operation (fig. 3 *A* and *B*). There was weakness of all muscle groups, easy fatigability and often a fine tremor. Reflex grasping became extreme. Especially evident, also, was hypotonicity, which was present at all times. Three weeks after operation an infant baboon began to show slight resistance to passive manipulation. During the next three months its ability to climb, run and feed itself improved (fig. 3 *C* and *D*), and there was still little spasticity. During the fifth and sixth months spasticity was observed as moderate or increasing. At the time of writing, when the animal is

19 months old, there are definite resistance to passive manipulation and with it contractures and increasing motor disability (fig. 4).

Three additional points of evidence have thus been brought out by the simultaneous ablation of both motor areas in the infant: first, that the motor cortex at the age of 3 weeks is functioning in the integration of motor acts; second, that within the boundaries of the motor areas this function is not completely localized, since unilateral ablation of

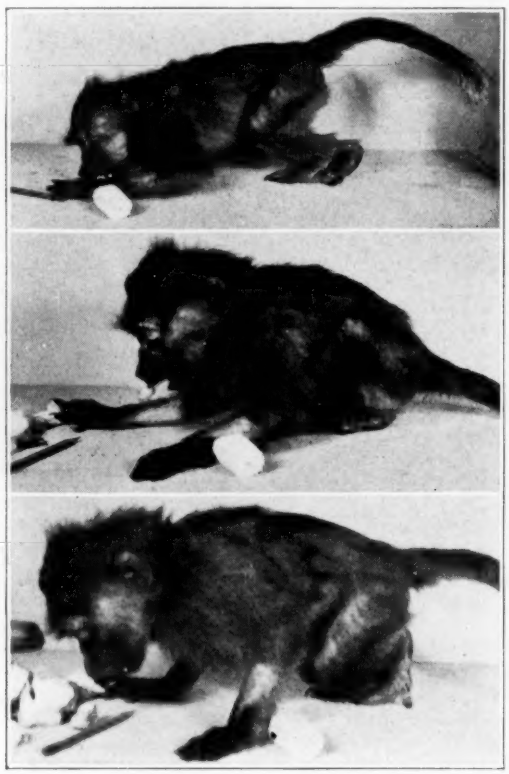


Fig. 4.—Photographs of the same baboon as that seen in figure 3 fourteen months after operation, showing marked difficulty in feeding. Note the "scissors" posture of the hindlegs, which is not present in figure 3.

these regions has almost no effect on motor performance and only complete removal significantly affects it, and third, that although paresis is present immediately after operation, no increase in resistance to passive manipulation appears until many weeks thereafter.

MOTOR DEFICIT IN THE INFANT CHIMPANZEE

In the chimpanzee the difference between the infant and the adult is even more marked, probably because the degree of motor deficit in

the adult chimpanzee following cortical ablation is much greater than that in the monkey and more closely resembles that in man. Two infant chimpanzees, of known age, the development of which had been studied from birth, have been available for this study.

The first (infant chimpanzee 2) had areas 4 and 6 on the left side removed during the fourth month of life, when motor performance was of the simplest order. At this age it lay as does a human infant, waving

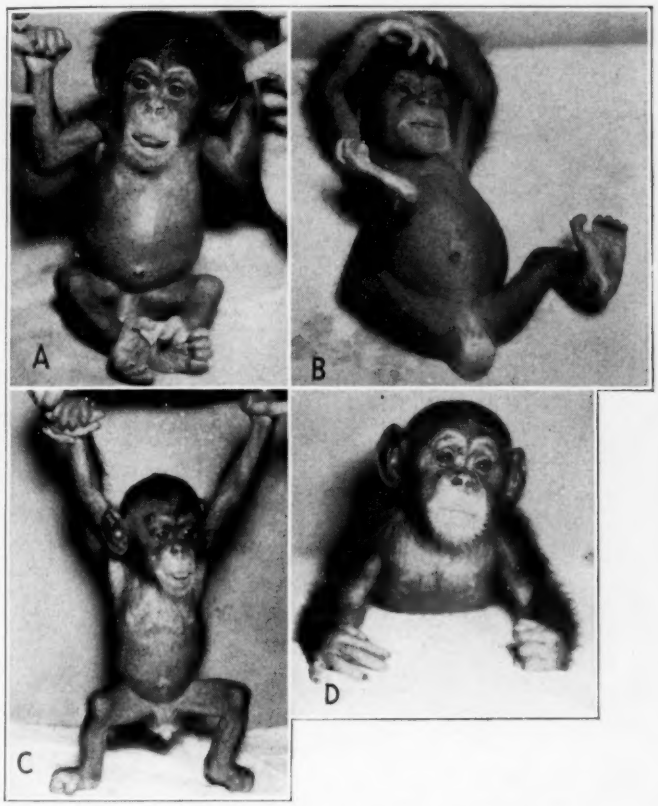


Fig. 5.—Infant chimpanzee 2. *A* and *B*, taken before operation, show normal posture and reflex grasping, at the age of 89 days. *C* and *D* were taken sixteen days after ablation of areas 4 and 6 on the left side, at the age of 133 days. Reflex grasping is still present; there is slight inequality of posture of the fingers in the right and left hands.

arms and legs freely, but unable to right itself or to grasp "voluntarily." Reflex grasping was strong. After operation there was at first no noticeable change in posture or in type of behavior, except that the spontaneous movements on the right side became less frequent than on the left (fig. 5). By the sixth month forced grasping had begun to

disappear on the normal side, but remained marked in the affected extremities for some weeks thereafter. During the sixth month posture also began to show differences. Hyperreflexia and a Rossolimo response then appeared on the right, but no increase in resistance to passive manipulation was noted until the eighth month of life.

The second chimpanzee (infant chimpanzee 3) had areas 4 and 6 on the left side removed during the tenth month of life, when it was already walking, climbing and feeding itself with its hands. Promptly

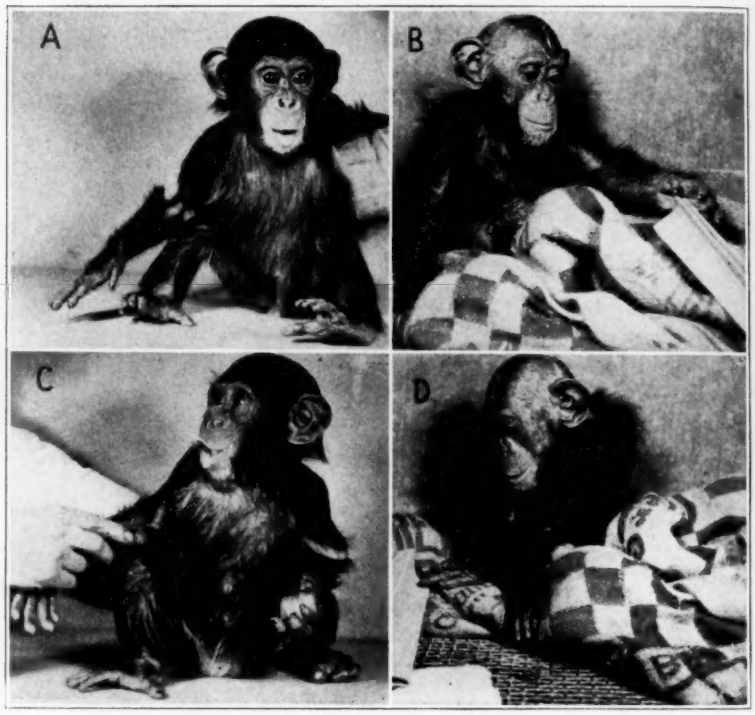


Fig. 6.—Infant chimpanzee 3, at the age of 10 months. *A* and *B* show normal posture; *C* and *D* were taken eleven days after ablation of areas 4 and 6 on the left side. The right arm is limp and is not used in "voluntary" prehension.

paresis appeared, somewhat less severe but in other ways like that of an older animal after a similar ablation (fig. 6). But there was no increase in resistance to passive manipulation. During the ensuing eight months the paresis diminished somewhat. The arm and hand continued to be held in the paretic position characteristic for man and chimpanzee; there was reflex grasping of the hand. The leg was raised high in walking, and the toes on this side were not used at all for the fine adjustment of balancing, as were those on the normal side. The knee jerk on the right was hyperactive, and a Rossolimo sign was present.

Now, when the animal is nearly 2 years old, resistance to passive manipulation is slightly increased on flexion at the knee and extension at the elbow (fig. 7). There are no contractures and no atrophy.

Thus, on comparing the effects of removal of the motor cortex in 2 young chimpanzees of different ages, the characteristics of development of both paresis and spasticity appear in sharp contrast in the two animals. One infant, operated on at a time when its normal motor performance was stereotyped, showed little change immediately thereafter. Later, when "voluntary" purposeful skilled motor acts began to appear in the normal extremities, those on the other side failed to develop and paresis became evident. Six months after this increased resistance to passive

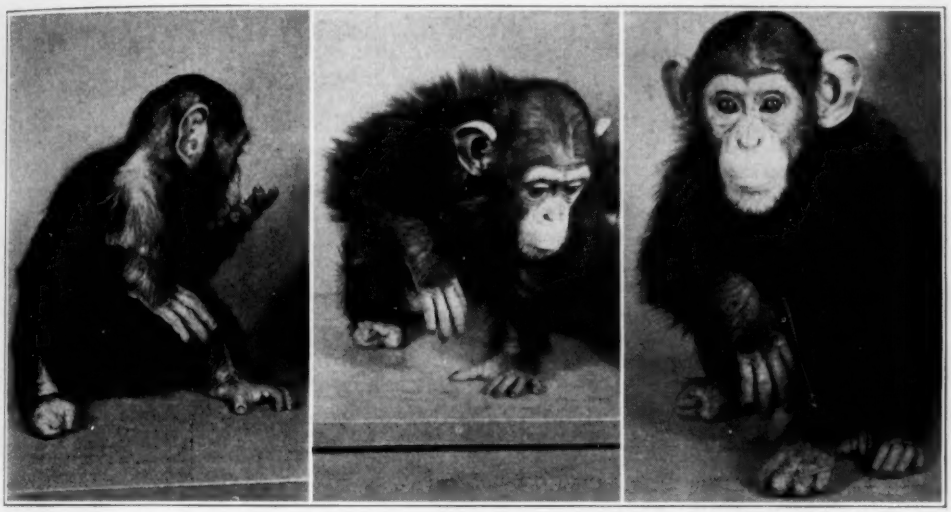


Fig. 7.—Photographs of the same chimpanzee as that shown in figure 6, at the age of 12 months, taken fifty-six days after operation. The right arm is now held in a "spastic" position.

manipulation was first noted. The second chimpanzee was operated on when walking and use of the hands for prehension were already established. This animal then showed definite paresis, although less extreme than that which would be seen in an older chimpanzee under the same conditions. The paresis persisted, and six months later slight increase in resistance to passive manipulation first appeared.

SUMMARY OF EXPERIMENTAL EVIDENCE

Comparison of motor deficits which appear after removal of known cortical areas in the infant and in the adult gives conspicuous evidence that the central nervous system of subhuman primates during infancy

exhibits greater capacity for reorganization and compensation than does that of the adult. The details may be summarized as follows:

1. In infancy unilateral ablation of the motor regions (areas 4 and 6) causes almost no immediate motor paresis, but during ensuing motor development of the animal the extremities on the side opposite the extirpation fail to acquire fine motor precision and motor paresis then becomes evident. It is never as great as that which appears in an older animal from which corresponding cortical areas have been removed.

2. The greater adequacy of motor function which appears after operation in infancy is due in large part to reorganization of cortical function; this is shown by the appearance of additional motor deficit on removal of the postcentral areas (areas 3-1-2, 5 and 7) or of the frontal association areas (areas 9-10-11-12) together with area 8, which in the adult have no such influence on motor status.

3. The two factors in motor deficit, namely paresis and spasticity, are more clearly distinguishable in the infant than in the adult. With development of the animal operated on in infancy, paresis appears first and is a negative quality, a failure of the abnormal extremities to acquire fine coordinate movements; much later, spasticity appears, as a positive element, an added increase in resistance to passive manipulation.

4. Both paresis and spasticity are immediately and ultimately much less severe if the ablation is made in infancy.

DATA ON HUMAN INFANTS

Examination of evidence obtained from human subjects indicates that in this primate form specificity and localization of function are also less in the cortex of the infant than in that of the adult. But, in the case of man, the evidence so far available is much less complete. The present data have been obtained in two ways: (1) by investigation of the cases and records of patients seen in the neurologic clinic of the Children's Hospital of Boston, and (2) by examination of the literature on paresis occurring in infancy and childhood. Relevant material obtained by these means is presented.

EXAMINATION OF CEREBRAL PALSIES IN MAN

Table 1 contains a summary of data obtained from the records of all cases of cerebral palsies seen at the neurologic clinic of the Children's Hospital of Boston since the beginning of that clinic. In the majority of the 233 cases, 149 in all, there was evidence of diffuse injury (presumably predominantly cortical) as shown by a bilateral motor deficit, but in 84 cases unilateral changes were shown which had been acquired after birth in 11 instances and presumably at or before birth in the remainder.

Neurologic examination was made of the 23 children with unilateral motor deficit who were being treated in the clinic at the time of this investigation. A comparison of the qualities of motor deficit in the

TABLE 1.—*Data in Cases of Cerebral Palsies*

	No. of Cases
Total number	233
Acquired before birth	219
Acquired after birth	14
Bilateral—total	149
Bilateral—acquired after birth	8
Unilateral—total	84
Unilateral—acquired after birth	11
Paresis on left	31
Paresis on right	50
Side of paresis not recorded	3

TABLE 2.—*Data on Cases of Birth Palsies*

Case No.	Age, Yr.	Paresis			Increased Resistance		Knee Jerk		Plantar Reflex	
		Face	Arm	Leg	Arm	Leg	Normal Side	Abnormal Side	Normal Side	Abnormal Side
1	5	0	++	++	0	0	+	++	—	+
3	5	0	++	++	0	0	+	++	—	+
5	6	+	++	++	Slight	Slight	+	+++	—	+
6	8	..	+	+	0	0	+	±	—	+
7	8	+	++	++	Slight	Slight	+	++	—	+
9	3	0	+	Slight	Slight	0	+	++	—	+
10	9	..	+	+	0	0	+	++	—	+
12	7	0	++	++	+	+	+	++	—	+
14	6	..	+	+	0	0	+	++	—	?
15	5	0	++	++	+	+	+	++	—	+
16	4	Slight	+	+	0	0	+	++	—	—
17	4	0	+	++	+	+	+	++	—	+
18	8	0	+	+	0	0	+	++	—	+
19	7	0	++	++	+	+	+	++	—	+
20	8	0	++	++	0	0	+	++	—	+
22	5	..	++	++	Slight	Slight	+	++	—	+

TABLE 3.—*Data on Cases of Early Hemipareses*

Case No.	Age, Yr.	Paresis			Increased Resistance		Knee Jerk		Plantar Reflex	
		Face	Arm	Leg	Arm	Leg	Normal Side	Abnormal Side	Normal Side	Abnormal Side
2	7	+	+++	+++	+++	+++	+	++	—	+
4*	10	+	+	+	0	0	+	+	—	+
8	3	+	++	++	++	++	+	+++	—	+
11	9	+	++	+	++	++	+	++	—	+
13	4	+	++	++	+++	+++	+	+++	—	+
21	6	..	++	++	++	+	+	++	—	+
23	7	+	++	++	++	++	+	+++	—	+

* This case is an exception, since resistance to passive manipulation was not increased.

group in which the abnormality was acquired at or before birth (table 2) with those in the group in which the deficit followed postnatal injury (table 3) shows striking dissimilarities in many respects. The two groups are, however, comparable since they are alike in the following

characteristics: (1) The average age of the group with earlier injury was 6.0 years, and that of the group with later injury was 6.5 years; (2) in each group plantar responses were abnormal on the affected side only; (3) sensory examination showed no striking differences between the two groups, only minor involvement of stereognosis or of two point discrimination being present in any instance.

In contrast, marked differences between the groups appeared with respect to the following qualities: (1) Paresis in the arm and leg was about equal in the two groups, and in no instance in either group was complete paralysis present. But, in every instance of late acquired paresis the face was involved, whereas in 9 of the 16 cases in which symptoms were acquired early the face was not involved. In only 2 instances was paresis of the face definitely present; in 1 it was "slight,"

TABLE 4.—*Data on Cases of Birth Palsies* *

Case No.	Age in 1936, Yr.	Early History	Paresis First Noted	Hemiparesis	Spasticity
1	5	Cord about neck; cyanosis	?	Right	Hypotonic
3	5	Low forceps delivery	Soon after birth	Left	None
5	6	Normal	With walking	Right	Slight
6	8	Forceps delivery	?	Right	Slight
7	8	Convulsions; normal delivery	With walking	Left	Slight
9	3	Cesarean delivery	With walking	Right	Hypotonia
10	9	Cesarean delivery	9 months	Left	Hypotonia
12	7	High forceps delivery	1 month	Left	Slight
14	7	Two transfusions	Since birth	Right	None
15	5	Cesarean delivery	4 months	Left	Slight
16	4	Induced labor	?	Left	None
17	4	Breech presentation	2-3 months	Left	Slight
18	8	Normal delivery	With walking	Right	None
19	7	Lumbar puncture at birth	With walking	Right	Slight
20	8	High forceps delivery	4 months	Left	None
22	4	Forceps delivery; convulsions	1 year	Left	Some

* In this table and in table 5, the histories were obtained from the hospital records.

and in 4 it was not recorded. (2) Spasticity, or increased resistance to passive manipulation, was strikingly different in the two groups. In each case this was examined at all joints in all extremities, and the normal and abnormal sides were compared. When present its characteristics were typical of cortical spasticity, resistance being most marked on flexion of the knee and extension of the elbow and on dorsiflexion of the wrist and ankle. In the cases of early acquired motor deficit there was almost no spasticity, as compared with that in cases of the late acquired deficit. In neither group was spasticity of 4 plus grade present in any instance (tables 2 and 3).

In table 4 are the data obtained from the records of the 16 patients who had birth palsies, and in table 5 those of the 7 patients acquiring hemiparesis after birth. Records were often inadequate, but whenever noted, the symptoms at birth and the time when paresis was first observed have been listed. In every instance in which hemiparesis was acquired after birth paresis appeared immediately or within a few days

after injury. The records did not state the time of appearance of spasticity in most instances. In contrast, in 7 of 16 cases in which injury was present from birth no motor defect was observed until walking was begun; in 4 cases the first deficit was recorded in the second to the fourth month; in 3 there was no note concerning the onset, and in only 2 were changes recorded as occurring soon after birth.

Case 4 (table 3) deserves special mention because in it alone, of the 7 cases of late acquired hemiparesis, there was no increased resistance to passive manipulation. This case was included with those of late acquired paresis because the hemiparesis first appeared immediately after an encephalogram was made, during the tenth year of life. However, the encephalogram was made at that time because the child had had convulsions since an early age and cortical atrophy was already present, as shown by roentgenograms taken at that date. This is a case, therefore, in which a second cerebral disturbance of some kind produced hemiparesis in a brain already abnormal, perhaps from birth. Interpretation of the pathologic condition from the neurologic findings is not possible, but it is not surprising that these findings did not conform entirely with those which followed late acquired injuries to presumably normal brains in the other 6 cases.

CLINICAL DATA FROM THE LITERATURE

On reviewing the literature on cerebral palsies, one finds much that may be correlated with the material just presented. There are many gaps unfilled, but careful examination of the papers from the time of Little,[6] Freud[7] and McNutt[8] to the reviews of Collier,[9] Ford[10] and Alpers and Dear[11] has corroborated many points.

In the majority of cases of cerebral birth palsies reported in the literature, as well as in those seen in Dr. Crothers' clinic, there was evidence of widespread destruction of the central nervous system as evinced by generalized motor deficit and often by mental retardation or idiocy. There were, however, a great number of cases in which motor

6. Little, W. J.: On the Influence of Abnormal Parturition, Difficult Labours, Premature Birth and Asphyxia Neonatorum, on the Mental and Physical Condition of the Child, Especially in Relation to Deformities, Tr. Obst. Soc. London **3**:293-344, 1862.

7. Freud, S.: Die infantile Cerebrallähmung, Vienna, A. Hölder, 1897.

8. McNutt, S.: Double Infantile Spastic Hemiplegia, with Report of a Case, Am. J. M. Sc. **89**:58-79, 1885.

9. Collier, J. S.: (*a*) Cerebral Diplegia, Brain **22**:373-441 (April) 1899; (*b*) The Pathogenesis of Cerebral Diplegia, ibid. **47**:1-21 (Jan.) 1924.

10. Ford, F. R.: Cerebral Birth Injuries and Their Results, Medicine **5**:121-194 (May) 1926.

11. Alpers, B. J., and Dear, R. B.: Hemiatrophy of the Brain, J. Nerv. & Ment. Dis. **89**:653-671 (May) 1939.

symptoms were confined to one side and in which at autopsy more or less circumscribed damage in one hemisphere was revealed.

The early histories in the latter group often had strikingly similar features. Previous reviews of larger series of cases, especially that of Ford,[10] offer thorough discussion of what is known of the etiologic, physiologic and anatomic factors in such cases. In all groups of cases of cerebral palsies difficult birth is more frequent than normal birth, as is prematurity. In the first days of life generalized convulsions appear in some, but not in the majority, of cases. Sometimes cyanosis and asphyxia are noted, but often the birth history is normal. The infant then usually is not seen for three, six or nine months (Cushing [12]) and is brought back to the physician because some one has noticed that one leg or arm does not move like the other. Usually this is not apparent until walking is attempted. The history may then record "inability to use the left leg since birth," but descriptions of neurologic examinations in which unilateral paresis or spasticity was recorded during the first few days of life cannot be found in the literature. On the other hand, there are frequent records of convulsions during the first days of life, and although these are usually generalized, they may be limited to one extremity or to one side. It seems probable, however, that in most instances, since hemipareses resulting from cortical lesions present at birth are not detected, they are not detectable until, with the normal development of complex behavior patterns, failure in development is made evident, as has been demonstrated in the young monkey or chimpanzee.

Evidence regarding the time of appearance of spasticity is more indefinite, and more confusing. There are many cases (Ford [10]) in which increased resistance to passive manipulation is not present early and in which it appears and increases with the development of the child. Often "stiffness" is the first abnormal symptom, and is noted by the family only when the child attempts to walk. No notes could be found correlating time of appearance of paresis with that of spasticity. Early flaccid paralysis of cortical origin has not been described, and marked spasticity accompanying hemiparesis during the first months of life has been rarely and ambiguously reported. Certainly, also, increased resistance to passive manipulation may appear and increase during the first years of life in patients in whom such spasticity was not present early, although it can be assumed that the lesion was present at birth.

In the literature another group of cases is also described in which rigidity or increase in resistance to passive manipulation is present from birth (Collier,[9b] Freud [7]). This group is clinically quite different from

12. Cushing, H.: Concerning Surgical Intervention for the Intracranial Hemorrhages of the New-Born, Am. J. M. Sc. **130**:563-581 (Oct.) 1905.

the group of cases of hemiplegia just described. The central nervous system is more extensively involved; at birth there is generalized rigidity or, often, opisthotonos, in which asphyxia sometimes seems to play a part. In these cases, first described by Little,[6] diplegia or quadriplegia develops. In some also athetosis and mental deficiency or bulbar speech appears. The lesion is always extensive and seems in many instances at least to involve subcortical as well as cortical structures. In these cases extreme spasticity, such as never appears in the first group of cases of hemiplegia, often develops in later childhood.

Much has been written on the differentiation of the two types of cerebral palsies just described. Ford discussed terminology and conflicting etiologic evidence. All writers have agreed that there are two syndromes resulting from early lesions, although terminology relating to the two types differs with various authors. One type is characterized anatomically by a lesion confined to cortical motor areas, as in the case of McNutt,[8] and clinically by hemiplegia or "bilateral hemiplegia,"

TABLE 5.—*Data in Cases of Hemiparesis Appearing at Early Age*

Case No.	Age in 1936, Yr.	Injury	Age of Injury, Yr.	Hemiparesis	Spasticity
2	7	Lead poisoning	2.0	Right	Marked
3	10	?	?	Right	None
8	3	Fell on stick in mouth	1.5	Left	Spastic
11	9	Scarlet fever	3.0	Left	Present
13	4	Fell on stick in mouth	2.5	Left	Moderate
21	6	Meningitis	0.75	Left	Present
23	7	Syphilitic meningitis	2.0	Right	Moderate

in which the arms are more seriously involved than the legs. As would be expected, because the lesion is more sharply localized, mental retardation is less often present in this type. In the second type there is anatomic evidence of widespread damage involving both hemispheres and often subcortical as well as cortical (Collier [9a]). Here the legs are more involved than the arms, and mental deficiency and signs of bulbar and striatal involvement are common. It is the children with this type of palsy who are often rigid at birth.

It is an accepted fact that the cerebral cortex of the newborn human infant has little function, although convulsions of a type indicating some cortical activity may occur. Moreover, since the pyramidal tracts are not myelinated at birth and are not myelinated completely until the age of from 9 to 24 months (Ford [10]), their functional absence in the normal infant does not produce spasticity. Apparently, complete anatomic absence of the tracts produces no more effect at this time, at least, Ford [10] described 2 cases of infants who at birth showed "all the reactions of normal babies" (page 137), but who later, at necropsy, were found to have been born without cerebral hemispheres. Two similar cases have

been seen recently in the New Haven Hospital.[18] In each case the child was apparently normal at birth, but hydrocephalus developed. In each, at an operation performed in order to coagulate the choroid plexus, it was observed that both cerebral hemispheres were virtually absent. These infants were not markedly spastic during the first months of life, although tendon reflexes were hyperactive. During the second half of the first year of life, definite spasticity has developed in each.

SUMMARY OF CLINICAL EVIDENCE

Clinical evidence strongly suggests that the central nervous system of the human infant exhibits a capacity for reorganization and compensation similar to that of the infant monkey or chimpanzee. 1. In the majority of cases of "birth palsies" there is evidence of diffuse and serious damage to the central nervous system. However, cases of discrete motor paresis, such as hemiparesis, exist and are not uncommon. There are many cases in which autopsy reveals that the extent of the lesion is far greater than would be expected from the amount of motor deficit.

2. Involvement of the face in early acquired paresis is rare but it is common in late acquired paresis. This could be due to a number of causes, but may be the result of greater ability of the ipsilateral face area or of other regions of the infant cortex to assume integration of motor acts. Perhaps, then, it is fair to deduce the converse, namely, that cortical derangement in the infant must be relatively great and generalized in order to be manifest and that slight deviations from normal anatomic arrangements are not followed by any detectable physiologic disturbance in the motor system, because of functional reorganization in the central nervous system.

3. Injury to cortical motor cells or pathways in the central nervous system may result in little or no immediately noticeable motor defect if the injury occurs at or before birth. But traumatic injury to the same areas (presumably) at a later date (9 months is the earliest age of late acquired paresis in this series) is followed by immediate paresis.

4. Spasticity may appear at some time after the appearance of paresis, since cases of anencephalic children have been reported in whom there was first noted failure to use the limbs in normal fashion, and in whom much later marked increased resistance to passive manipulation appeared and increased progressively.

5. Another syndrome exists in which generalized increase in resistance to passive manipulation is present at birth. This is often associated with anoxemia and cyanosis. In cases of this type diplegia (not bilateral hemiplegia) often develops. At autopsy extensive cortical and subcortical destruction may be shown.

---

13. Dr. William J. German performed operation in these cases and permitted me to examine the patients and to include the data in this paper.

6. Neither paresis nor spasticity from cortical motor deficit is as extreme when acquired early as when acquired late in childhood. In neither type is spasticity as great as it is when acquired by the adult.

COMMENT

In the monkey, chimpanzee and man, age has, therefore, an important influence on the development of paresis and of spasticity following injury to the cerebral cortex. In each form less motor deficit results from a cortical injury which occurs at an early age. A relative functional nonspecificity of cortical areas is partially responsible for this greater compensatory power in infancy, since in the complete or partial absence of the true motor fields (areas 4 and 6) the intact cortical regions of the infant—the remaining parts of areas 4 and 6, the postcentral gyrus (areas 3-1-2) or the frontal assocation areas (9-10-11-12) and visual fields (area 8)—assist in the integration of skilled motor acts to great degree, whereas in the adult, after the same procedures, much less coordinate motor ability is recovered. According to Conel,[14] there is actual anatomic evidence which may be correlated with this functional nonspecificity, since, although all the cellular elements and layers of the cerebral cortex observed in the adult may be identified in the cortex of the newborn human infant, he has found that in the infant the cells of different regions are more uniform in size and structure. Thus, the Betz cells of the newborn infant are described as rounder and smaller than those of the adult. The Nissl structure is less well differentiated, and the Betz cells of area 4 cannot often be distinguished from the large round cells of the fifth layer in area 6.

On the other hand anatomically, no new organization is necessary for the functional reorganization, since, as shown originally by Betz [15] and confirmed by Levin and Bradford,[16] there are Betz cells in the postcentral gyrus and area 6 possesses large motor cells in addition to islands of Betz cells.[17] The pattern localization in the cortex recently emphasized by Woodburne [18] exists as background for whatever reorganization

14. Conel, J. L.: The Cortex of the Newborn, in The Postnatal Development of the Human Cerebral Cortex, Cambridge, Mass., Harvard University Press, 1939, vol. 2.

15. Betz, W.: Anatomischer Nachweis zweier Gehirncentra, Centralbl. f. d. med. Wissensch. **12**:578-580 and 594-599, 1874.

16. Levin, P. M., and Bradford, F. K.: The Exact Origin of the Cortico-Spinal Tract in the Monkey, J. Comp. Neurol. **68**:411-422 (June) 1938.

17. Kennard, M. A.: Corticospinal Fibers Arising in the Premotor Area of the Monkey as Demonstrated by the Marchi Method, Arch. Neurol. & Psychiat. **33**: 698-711 (April) 1935.

18. Woodburne, R. T.: Certain Phylogenetic Anatomical Relations of Localizing Significance for the Mammalian Central Nervous System, J. Comp. Neurol. **71**:215-257 (Oct.) 1939.

takes place in either a younger or an older animal. In connection with this it must be remembered that, although recovery of the infant is much greater than that of the adult, some recovery always takes place in an adult also (following partial lesions of areas 4 and 6, at least), and that this is due in part to the remaining portions of areas 4 and 6.[3]

The factors which underlie the increase of motor impairment (whether due to spasticity or to paresis) which develops during many months following cortical injury in the infant are not yet entirely clear, but the progress of myelination seems to be important. Myelination is generally supposed to be correlated with function, and, since it is known that in neither monkey nor man (Ford,[10] Artom [19]) are corticosubcortical tracts completely myelinated at birth, it is not surprising that discrete "voluntary" motor acts are absent in the newborn infants. There is however, some cortical activity at birth, for generalized movements can be obtained from stimulation of the motor cortex at this time (Hines,[1] Kennard [4]). In addition, local convulsions which may be cortical occur in human infants, and there is some immediate deficit if all the motor cortex is removed from the monkey at this age.

Myelination of the corticospinal tract arising from area 4 occurs before that of other cortical efferent pathways. Functionally, this may be correlated in the monkey with the appearance of "voluntary" prehension during the ninth week of life, in the chimpanzee with the use of the hands and with walking and crawling after the fifth or sixth month, and in the human infant with balancing, walking, and the like, after the ninth month. If, for any reason, the pyramidal tract is unable to function at this time, skilled and coordinate motor performance will not develop completely and impairment appears as failure to learn the skilled acts of which the normal motor system is capable. In the monkey and chimpanzee at least, and probably in man also, there is in such cases no spasticity at this stage of development.

Full functional coordination does not appear in the normal infant macaque until the second half of the first year of life, in the chimpanzee until the third year and in man until several years later. The time of myelination of the extrapyramidal cortical systems of area 6 and of the frontal association areas is not definitely known (Langworthy [20]), except that it occurs later than that of area 4. At any rate, it is probably during this period of myelination that spasticity develops if the cortical extrapyramidal areas have been previously removed. These considerations make it possible to postulate that spasticity is a "release phenomenon." In the adult, removal of cortical areas (area 6 or 4-s), which normally

19. Artom, G.: Untersuchungen über die Myelogenese des Nervensystems des Affen, Arch. f. Psychiat. **75**:169-234, 1925.

20. Langworthy, O. R.: Medullated Tracts in the Brain Stem of a Seven Month Human Fetus, Contrib. Embryol. **20**:37-52, 1930.

integrate skilled coordinate movements, results in "release" of other pathways (cortical or subcortical), thus causing spasticity. Removal of these same areas from the infant cortex has no such effect until other reflex circuits (cortical or subcortical) become functionally active, presumably by their myelination. Then, in the absence of the "higher" controlling mechanism, spasticity appears.

There is at present no conclusive evidence concerning the remaining tracts which integrate spastic motor performance in the absence of cortical motor areas. If ablation of the motor cortex of a monkey is made in infancy, the existence of other cortical regions—one intact motor area, areas 8 to 12 or areas 3-1-2—will prevent the appearance of spasticity, but not if it is made in adult life. It is reasonable to suppose that the action of these regions on subcortical motor centers is prevention of "release" and spasticity.

CONCLUSIONS

In primate infants (man, chimpanzee or monkey) the development of paresis and spasticity has been shown to be related to defects in the functional and anatomic development of the central nervous system. Evidence obtained from experimentation on subhuman primates shows that the central nervous system of the infant is potentially different from that of the adult, as manifested by the motor deficits which appear after known cortical ablations. This is corroborated by clinical evidence obtained by the study of the human infant.

1. The absence of cortical motor areas is not accompanied by any marked and noticeable motor deficit in the infant before complex skilled motor activity has developed.

2. Paresis is first seen after ablation of motor cortical areas in the infant at a time when normally skilled coordinated movements should appear.

3. Spasticity (increased resistance to passive manipulation) begins to appear much later than paresis, possibly at the time when there is functional organization of certain subcortical motor pathways.

4. In the monkey the greater adequacy of motor function which develops after precentral ablations in infancy is due in part to reorganization of cortical function, since additional motor deficit appears in such animals after subsequent ablation of postcentral or frontal association areas.

5. The paresis, and to a much greater extent the spasticity, is always less severe in all primates if the causative lesion occurred in infancy.

SPECIAL ARTICLES

SYNDROME OF FINGER AGNOSIA, DISORIENTATION FOR RIGHT AND LEFT, AGRAPHIA AND ACALCULIA

LOCAL DIAGNOSTIC VALUE

JOSEF GERSTMANN, M.D.*

NEW YORK

This paper is concerned with the syndrome, described by me some years ago, of finger agnosia, disorientation for right and left, agraphia and acalculia, appearing as a result of a cerebral lesion located in the transitional area of the lower parietal and the middle occipital convolution.

In 1924 I first described the symptom of primary elective disability for recognizing, naming, selecting, differentiating and indicating the individual fingers of either hand, the patient's own as well as those of other persons, and called the condition "finger agnosia." Subsequent to this gnostic disorientation with respect to the fingers, restriction in their separate kinetic realization not infrequently occurs. I also showed that the symptom of finger agnosia is characteristically associated with disorientation for right and left in respect to the patient's own body, as well as that of other persons, with special reference to the hands and fingers. The symptoms tend to appear in varying degrees of development. Furthermore, I found that these symptoms are commonly combined with an isolated disturbance of writing—agraphia—and an isolated disability for calculation—acalculia—of differing intensities and of definite character. All these symptoms group themselves pathologically into a well circumscribed cerebral syndrome. Investigations in a large number of cases of this type have so far failed to reveal any evidence of psychic, particularly of intellectual, disorder; of aphasia, apraxia or other manifestation of agnosia, or of motor or sensory changes to which the symptom complex of finger agnosia or its individual features could be related. This syndrome has therefore been

Read at the Ninety-Fifth Annual Meeting of the American Psychiatric Association, Chicago, May 11, 1939.

* Formerly Professor of Neurology and Psychiatry, the University of Vienna; at present at the Neurological Institute of New York, Neurological Division of Vanderbilt Clinic.

considered primary. It was eventually proved, in the sense of the assumption expressed in my first paper, that the syndrome of finger agnosia, confusion of right and left, agraphia and acalculia is a result of a lesion located in the parieto-occipital region of the brain, namely, in that part which corresponds to the angular gyrus in its transition to the second occipital convolution.

A considerable literature followed the description of the syndrome. A number of authors in different countries (Herrmann and Pötzl, Schilder, Kroll, Lange, Marburg, von Rad, Schuster, Pineas, Klein, van Woerkom, Embden, Ehrenwald, Laubenthal, Conrad, Engerth, von Stockert, Pedersen, Muncie, von Angyal, Wagner, Mayer-Gross, Mussio-Fournier and Rawak, Nielsen, Strauss and Werner) have made careful studies. It may be said that in all the publications up to the present my data on finger agnosia and its association with disorientation for right and left and isolated disorder in writing and calculating as a special cerebral symptom complex have been confirmed so extensively and uniformly that the syndrome may now be considered as established.

The syndrome has proved not to be rare, when looked for. Since my first observation, I established its presence in varying degrees of development in a considerable number of cases of cerebral lesions in the region mentioned, the syndrome appearing either at the beginning, in a primary elective form, or as a residual condition or a restitution stage after the regression of a more complex clinical picture. A considerable number of competent observations have dealt partly with the syndrome of finger agnosia in the narrower sense and partly with its phenomenologic variants. The latter have already given occasion to the differentiation of clinical types of finger agnosia. Thus, Schilder undertook a subdivision into the following types, to each of which he attributed a distinct localizing value: finger agnosia (in the narrower sense), optic finger agnosia, constructive finger apraxia, apractic disturbance of finger selection and finger aphasia. Lange suggested a subdivision into the following varieties: an optic agnostic, a speech-amnestic, a constructive apractic and a pure apractic form.

The clinical picture of finger agnosia is characteristic. A patient with this disability cannot orient himself with regard to the individual fingers of either hand (his own as well as those held out by the examiner). He cannot recognize them in any way corresponding to the normal; he cannot differentiate his fingers (thumb and index, middle, ring and little fingers) at all, or not fully; he cannot name them correctly, cannot indicate specific fingers on command and cannot imitate given finger postures of the examiner, and he commits striking errors in appropriate tests. This occurs in spite of the patient's theoretic knowledge of the hands and fingers, in spite of the absence of disturbance

of general optic and tactile comprehension, in spite of sufficient vision to guide him and in spite of the absence of any interfering motor or sensory disorders. It is noteworthy that mistakes with regard to the three middle fingers are usually more pronounced than those relating to the thumb and the little finger. The patient most often does not become aware of his errors spontaneously and is helpless in controlling them. The phenomenon of finger agnosia, representing a primary disturbance of recognition and orientation confined to the fingers of both hands, may also, according to the degree of its development, be accompanied secondarily by a certain lack of freedom in the individual actions of the fingers and by difficulty in their separate practic realization. As far as the limbs (including the toes) and the other parts of the body are concerned, ability to recognize them and to orient as to them remains essentially unaltered. It is as though, in finger agnosia the so-called body scheme, the postural model of the body—that is, the image which a person normally has of his body and the spatial relation of its parts—were affected by a focal cerebral lesion in one sphere only, and, indeed, the most significant, differentiated and vulnerable one—the sphere concerned with the individual fingers.

Closely bound up with finger agnosia, in my experience, is more or less extensive disturbance of the capacity for recognition of right and left and orientation as to laterality with respect to the patient's own body and that of others, particularly as regards the hands and fingers. This disturbance is confined to the body sphere exclusively; that is, it does not apply to the ability to distinguish right from left in space and with respect to objects outside the body. Although finger agnosia is more often shown in tests requiring distinction between right and left, the symptom manifests itself irrespective of whether laterality is being tested. However, involvement of appreciation of right and left renders the test for finger agnosia more difficult for the patient. Disorientation for right and left results in difficulty and uncertainty in the choice of sides for actions necessitating a conception of right and left—as, for example, when the patient is commanded to grasp or to point with the hands and fingers to contralateral parts of the body.

Finger agnosia and disorientation for right and left are commonly, or at least in the great majority of cases, associated with an isolated disability or inability to write—so-called pure agraphia. This may either involve writing of words only (verbal agraphia) or impair writing of letters (literal agraphia) as well. It appears peculiar to this type of agraphia that spontaneous writing and writing from dictation are as a rule considerably more disturbed than copying from a sample.

The fourth characteristic feature of the syndrome is an isolated disability or inability to perform calculations—so-called acalculia. This may involve only arithmetical operations with more or less complex

numbers, or it may incapacitate the patient in operating with even simple numbers. There is a corresponding disturbance of the ability to convert more complex numbers into simpler ones, or vice versa. The significance of the position of the digit within a given complex figure is not realized; accordingly, the patient is disoriented regarding the sequence and the decimal values of the digits within a figure.

The coincidence of finger agnosia and disorientation as to right and left, on the one hand, and agraphia and acalculia, on the other, is fairly understandable if one remembers what an important part is played by the individual fingers and their right and left laterality in acquisition of the functions of writing and calculating. The function of writing is inconceivable without the highly integrated level of morphologic and physiologic differentiation of fingers that has developed in man, and continuation of intact ability to write is incompatible with disintegration of this development. Fingers supply the first aid in learning to calculate, as is commonly known. The first arithmetical operations of children are performed on the fingers of each hand, while the toes do not take part. In the counting operations of primitive people, and probably in the whole system of numeration, fingers and hands seem to play an important role. It is significant in this connection, for example, that the word "digit" means both "finger" and any one of the Arabic numerals. This is undoubtedly not accidental. It suggests an intimate relationship between differentiation of fingers and calculation.

My observations have convinced me that occurrence of isolated agraphia and acalculia [1] may be primarily, or perhaps even exclusively, a clinical peculiarity associated with finger agnosia and the accompanying disorders of directional selection (to right and left). I have, at least thus far, not observed the coincidence of disturbances of recognition, selection, naming and pointing with the individual fingers, as revealed in the phenomenon of finger agnosia, and disturbances of writing and calculating of another category, such as those usually associated with certain defects of an aphasic, apractic or allied type. However, this does not mean that in each case of isolated agraphia and acalculia the finding of finger agnosia with disorientation for right and left is inevitable, even if such a possibility, from my experience, cannot be wholly denied. At all events, it is essential in any case of isolated disturbance of the acts of writing and counting not to neglect search for the symptom of finger agnosia and for right and left disorientation (and other selections of direction).

1. For investigators who dispute the validity of the distinction of isolated agraphia and acalculia and prefer to merge all disturbances of the acts of writing and calculating with other cortical disorders, it may be mentioned that in making this statement I mean not so much to express classificatory tendencies as primarily to draw attention to the combination of finger agnosia and agraphia and acalculia as manifested in an isolated form.

With the syndrome under discussion may be grouped various other clinical symptoms, such as constructive apraxia, amnestic reduction of word finding, a certain, usually insignificant, disturbance of the capacity to read, impairment of color perception, absence of optokinetic nystagmus and disturbance of equilibrium. Except for constructive apraxia, these manifestations, because of their relatively variable occurrence and the proportionately slight degree to which they are found (as compared with the cardinal symptoms of finger agnosia, disorientation for right and left, agraphia and acalculia), can undoubtedly be regarded as arising from involvement of border or neighborhood tissue. The simultaneous occurrence of right homonymous hemianopia or hemiamblyopia appears to be a constant feature.

The general psychic condition of a patient with the typical syndrome of finger agnosia and associated symptoms is remarkably good. The patient is usually cooperative, alert and mentally clear. Except for the reflected influence of the syndrome, the intelligence is essentially unaltered, unless an intercurrent cerebral lesion interferes. The patient is correctly oriented for place and person. However, he may be more or less disoriented for time. This disturbance, which is in remarkable contrast to the patient's general mental condition, is to be considered merely as a result of his disability to calculate and comprehend numbers and their handling. The ability to calculate seems to me to be an indispensable prerequisite for proper orientation in time. The personality as a whole is primarily intact. There is impairment only of a special basic function, a special tool in the service of the personality. The basic disorder underlying the various manifestations of the syndrome remains hypothetic.

In my first case of finger agnosia, that of a woman aged 52 who previously had suffered a cerebral accident, I concluded that a circumscribed softening in the lower part of the left parietal lobe, namely in the angular region, was probable, without, however, being able, in the absence of an autopsy, to make a more exact localization at the time. This assumption was soon confirmed by Herrmann and Pötzl in a case of tumor of the brain in which an autopsy was performed. In this case, in which the complete syndrome had been shown, the parieto-occipital region, particularly the angular gyrus and its area of transition to the second occipital convolution, was the seat of the lesion. Since then, the observations made at autopsy, both by me and by other investigators, in a series of cases of this syndrome, have established and corroborated the localization of the lesion in the region of the lower part of the parietal lobe and the middle occipital convolution directly adjoining. In the cases in my own observation in which autopsy was performed, the syndrome under discussion was present in typical form, and a few may be cited.

The first case was one of cerebral glioma involving a considerable portion of the parieto-occipital convexity, with complete destruction of the transitional region between the angular gyrus and the middle occipital gyrus. In a second case, a focal cerebral softening of several months' duration involved this transitional region; the onset had practically coincided with the appearance of the symptom complex. In a third case a glioma, approximately the size of an orange and soft for the most part, was located in the parieto-occipital region, the damage extending to the posterior part of the lower left temporal convolution. In a fourth case a focal softening was confined to the region of the left angular gyrus and the area of transition to the middle occipital convolution.

Other examples could be cited. It may be emphasized that in all cases autopsy confirmed the clinical diagnosis of a focal lesion in the region of the lower part of the parietal lobe and the region of transition to the occipital lobe.

It can accordingly be stated (with the reserve appropriate to an interpretation of localization) that the syndrome of finger agnosia, disorientation for right and left, agraphia and acalculia must be considered as related to a lesion of a common apparatus in the region of the parieto-occipital convexity, particularly in that part which is represented by the transitional region of the angular and the middle occipital convolution.

A survey of my own material and that of others reveals that the development of the syndrome differs, presumably in correlation with the extent of the focal lesion. Indeed, two forms of manifestation can be distinguished: a primary and a secondary. In the first type there is direct primary development of the syndrome. In the other type the clinical picture is dominated first by a more extensive complex of signs and symptoms; only after a certain regression of these symptoms does the syndrome of finger agnosia and its related disturbances become apparent—as if it had previously been concealed by too many other changes; the syndrome thus presents itself, in the second type, as a restitution stage in a more complex clinical picture, in which formerly other features had prevailed. I have repeatedly observed cases in which, after an apoplectic seizure, definite sensory, or pseudosensory, aphasia (in combination with apractic, tactile agnostic and alexic manifestations) was first seen, and later, after gradual recovery from the sensory aphasic disturbances (with extensive restoration of the reading capacity) and decline of other changes, the symptom complex of finger agnosia became manifest and remained as a residual condition, together with right homonymous hemianopia, which had existed from the beginning. In all these cases it was noteworthy that at the height of the aphasia, in tests for execution of oral commands or naming of objects, the disturbance was most pronounced when the individual fingers of either hand were concerned. This dissociation with the results in carrying out other commands and in naming other objects (even other parts of

the body) was striking. After recovery from the aphasia and appearance of the finger agnosia it became evident that the finger agnosia had existed from the beginning but had not been recognizable because it had been concealed by sensory aphasic manifestations.

Evidently, the primary or secondary appearance of the syndrome of finger agnosia in the cases referred to was dependent on the extent and the activity of the parietal or parieto-occipital lesion. In the one group the focal lesion may be less severe and may be confined mainly to the transitional region of the angular and the second occipital convolution. In the other group the process may be of greater intensity and at first more extensive, affecting also the parietal or the parieto-temporal region. At all events, it may be assumed in the case of the second group that the accentuated effect of the lesion in the region of transition of the lower part of the parietal lobe and the middle occipital convolution represents the topical factor, which is of determinative importance for the appearance and the frequent persistence of the syndrome. It can generally be said that the more limited the focal lesion (provided it is appropriately situated), the more suitable the conditions for the syndrome to appear electively. In other words, the basic function underlying the syndrome will alone be affected. In this case, the syndrome will dominate the clinical picture from the beginning. The more extensive the focal lesion, the more will other pathologic (even gross) manifestations result and conceal the finer syndrome of finger agnosia with disorientation for right and left, agraphia and acalculia. Only with recovery from the massive clinical manifestations will the more differentiated symptom complex become apparent, and finally dominate the picture.

The close relation of the phenomena constituting the syndrome is not only topical, but evidently genetic and pathophysiologic as well. One must, therefore, postulate a uniform pathophysiologic alteration corresponding to the uniform localization. This aspect of the problem is not yet solved. It culminates in the question of what damage to function consolidates the individual elements of the syndrome as a basic disturbance—as a fundamental unit. The solution of this problem has been attempted by various investigators with arguments of varying degrees of impressiveness. Yet it cannot be said that thus far a conclusive solution of the problem has been provided, however suitable the explanations may be for furthering comprehension of the pathophysiologic mechanism of the syndrome in many respects. Further investigations remain to be made.

The pathophysiologic basis of the syndrome is therefore, for the present, unsolved. However, the localizing value of the syndrome may

now be considered as proved. This statement is based on the observed material thus far collected, comprising partly cerebral tumors and partly focal cerebral softenings. In particular, the practical utilization of the syndrome in the local diagnosis of compressive lesions in the lower part of the parietal lobe or the transitional zone of the parieto-occipital region, respectively, should be emphasized. The symptom complex of finger agnosia has already pointed to the diagnosis of the site of a large number of tumors in the area of the brain under discussion, and on this suggestion surgical procedures have been defined with success. The value of this mode of localization has stood the test in a considerable series of cases of cerebral tumors in which the location of the lesion in the angular gyrus or the transitional region between the angular and the second occipital gyrus, respectively,[2] was verified not only by biopsy but also by autopsy. In recapitulating actual experiences, it may be said that in cases of cerebral tumors the syndrome, when characteristically marked, has consistently proved itself reliable for purposes of topical diagnosis; when removal of the tumor was possible by operation the individual symptoms receded more or less completely in time.

The localizing value of the syndrome is significantly emphasized by the fact that the syndrome of finger agnosia is represented in the brain unilaterally, and that (as in aphasia and apraxia) it is associated with a correspondingly located lesion in the dominant side of the brain, that is, the left hemisphere in right-handed persons. The aforementioned case of Herrmann and Pötzl, in which the tumor was localized in the transitional zone of the right parieto-occipital region, is the only exception. It must, however, be noted that this case was that of an ambidextrous person. This suffices to explain the localization of the focal lesion in the right cerebral hemisphere, and at the same time decidedly reduces the seemingly exceptional significance of the case. Otherwise, both in the material which I observed and, as far as I know, in that studied by others, there have been only correspondingly located lesions in the left side of the brain.

In conclusion, one more statement may be made which has possible significance. I originally defined finger agnosia as a circumscribed disturbance of the capacity for recognition and orientation in one section of the body sphere only, a formulation expressed in the title of my first communication. There is no doubt that finger agnosia presents itself in

2. It is true that, some years ago, Klein reported a case of a clearly characterized syndrome of finger agnosia, disorientation for right and left and disturbance in writing and calculating in which at operation the tumor was observed in the middle part of the left parietal lobe (near the cortical border). One must assume here, however, that in the apparently extensive area of activity of the tumor the zone transitional in the parieto-occipital region was also involved.

this way.[3] It is noteworthy, however, as Schilder emphasized some years ago, and with whose opinion one must agree, that finger agnosia is the only disturbance of recognition and orientation with respect to the patient's own body, as well as that of others, which can be found as a result of a circumscribed cerebral lesion. I have not yet observed undoubted disturbances of recognition and orientation with regard to other sections or limbs of the body, other forms of so-called autotopagnosia either of general nature or of isolated character, associated with a focal cerebral lesion,[4] although I have sought them for many years. Evidently, except for finger agnosia, disturbances of recognition and orientation concerned with the rest of the body occur only with more expansive, particularly more diffuse, cerebral processes. The latter, moreover, usually result in psychic disturbances, in aphasic, apractic and other agnostic manifestations, behind which disturbances of recognition and orientation in the body sphere—extensive or limited—for the most part are not discernible. Finger agnosia, however, with disorientation for right and left and the other manifestations, is usually caused by a local lesion affecting the area of transition in the parieto-occipital region. The focal character of the cerebral lesion is the factor that explains the development of the syndrome and its isolation from other changes which might veil it or conceal its individual features.

BIBLIOGRAPHY

Gerstmann, J.: Fingeragnosie: Eine umschriebene Störung der Orientierung am eigenen Körper, Wien. klin. Wchnschr. **37**:1010-1012, 1924.

Herrmann, G., and Pötzl, O.: Ueber die Agraphie und ihre lokaldiagnostischen Beziehungen, Berlin, S. Karger, 1926.

Gerstmann, J.: Fingeragnosie und isolierte Agraphie, ein neues Syndrom, Ztschr. f. d. ges. Neurol. u. Psychiat. **108**:152-177, 1927.

3. If one attempts to explain finger agnosia on the basis of the concept of the so-called body scheme, one might speak of a disturbance of the corresponding part of the body image, of a dissociation of the section of the body scheme appertaining to the fingers—as if the optic-tactile-kinesthetic image for the individual fingers were split off from the total body image, the finger scheme from the total body scheme.

4. Some years ago I had under my observation a hypertonic patient with clinical manifestations pointing to a focal softening in the left parietotemporo-occipital region in whom the discrepancy between the capacity for recognition and orientation with respect to the hands and fingers and that with respect to other parts of the body was conspicuous. While in this woman the finger agnosia, which was accompanied by a correspondingly intense disturbance of orientation for right and left and almost complete incapacity to write or calculate, was so marked that in repeated examinations not only did no correct reaction result, but occasionally (though sensibility was not disturbed) the individual fingers, and even the hands, were not noticed at all, nevertheless perception and orientation for the remaining parts of the body remained intact.

Herrmann, G.: Beiträge zur Lehre von den Störungen des Rechnens bei Herderkrankungen des Okzipitallappens (Akalkulie Henschen), Monatschr. f. Psychiat. u. Neurol. **70**:193, 1928.

Kroll, M.: Die neuropathologischen Syndrome, Berlin, Julius Springer, 1929.

Gerstmann, J.: Zur Symptomatologie der Hirnläsionen im Uebergangsgebiet der unteren Parietal- und mitteleren Occipitalwindung, Nervenarzt **3**:691-695, 1930.

von Rad, C.: Kasuistischer Beitrag zur Symptomatologie der Herderkrankungen in der Übergangsregion des Parietal- und des Occipitallappens, Ztschr. f. d. ges. Neurol. u. Psychiat. **131**:273-288, 1930.

Lange, J.: Fingeragnosie und Agraphie (ein psychopathologische Studie), Monatschr. f. Psychiat. u. Neurol. **76**:129-188, 1930.

van Woerkom, W.: Psychopathologische Beobachtungen bei Stirnhirngeschädigten und bei Patienten mit Aphasien. Eine zusammenfassende Darstellung, Monatschr. f. Psychiat. u. Neurol. **80**:274, 331, 1931.

Marburg, O.: Scheitellappenerweichung unter dem Bilde eines Pseudotumor cerebri (Zugleich ein Beitrag zur Frage der Fingeragnosie ohne Agraphie), Arb. a. d. neurol. Inst. a. d. Wien. Univ. **33**:1-13, 1931.

Schilder, P.: Fingeragnosie, Fingerapraxie, Fingeraphasie, Nervenarzt **4**:625-629, 1931.

Localization of the Body Image (Postural Model of the Body), A. Research Nerv. & Ment. Dis., Proc. **13**:466-484, 1932.

Wagner, W.: Ueber Raumstörung, Monatschr. f. Psychiat. u. Neurol. **84**:281-307, 1932.

Zutt, J.: Rechts-Linkstörung, konstruktive Apraxie und reine Agraphie. Darstellung eines Falles: Ein Beitrag zur Pathologie der Handlung, Monatschr. f. Psychiat. u. Neurol. **82**:253 and 355, 1932.

Laubenthal, F.: Zur psychologischen Analyse von Kranken mit einem Syndrom der linken Parieto-Occipitalgegend, Arch. f. Psychiat. **99**:633-682, 1933.

Vlavianos, G.: Zur Symptomatologie des Parieto-Occipitalhirnes, Wien. med. Wchnschr. **83**:502-505, 1933.

Klein, R.: Ueber die Funktionen des Parietallappens, Nervenarzt **6**:1 and 67, 1933.

Engerth, G.: Zeichenstörungen bei Patienten mit Autotopagnosie, Ztschr. f. d. ges. Neurol. u. Psychiat. **143**:381-402, 1933.

von Stockert, F. G.: Das Gerstmannsche Syndrom der Fingeragnosie, mit besonderer Berücksichtigung der Sprach- und Schreib-Störung, Monatschr. f. Psychiat. u. Neurol. **88**:121-151, 1934.

Mussio-Fournier, J. C., and Rawak, F.: Glioblastome de l'hémisphère gauche avec syndrome de Gerstmann: Réaction mélanophorotrope sur la grenouille par l'urine de la malade, Rev. neurol. **2**:681-685, 1934.

Muncie, W.: Finger-Agnosia (Gerstmann), Bull. Johns Hopkins Hosp. **57**:330-342, 1935.

Mayer-Gross, W.: Some Observations on Apraxia, Proc. Roy. Soc. Med. **28**:66-72, 1935.

von Angyal, L.: Beiträge zur Symptomatologie, Lokalisation und hirnpathologische Auffassung des Gerstmannschen Syndroms, Ztschr. f. d. ges. Neurol. u. Psychiat. **156**:245-264, 1936.

Lange, J.: Die agnostischen Störungen, in Bumke, O., and Foerster, O.: Handbuch der Neurologie, Berlin, Julius Springer, 1936, vol. 10, p. 876.

Scheller: Syndrom des Parieto-Occipitallappens, Zentralbl. f. d. ges. Neurol. u. Psychiat. **81**:109, 1936.

Guttmann, E.: Congenital Arithmetic Disability and Acalculia (Henschen), Brit. J. M. Psychol. **16**:16-35, 1936.

Pedersen, O.: Zur Kenntnis der Symptomatologie der parieto-occipitalen Übergangsregion, Arch. f. Psychiat. **105**:539-549, 1936.

Nielsen, J. M.: Gerstmann Syndrome: Finger Agnosia, Agraphia, Confusion of Right and Left and Acalculia, Arch. Neurol. & Psychiat. **39**:536-559 (March) 1938.

Strauss, A., and Werner, H.: Deficiency in the Finger Schema in Relation to Arithmetic Disability (Finger Agnosia and Acalculia), Am. J. Orthopsychiat. **8**:719-725, 1938.

Werner, H., and Strauss, A.: Problems and Methods of Functional Analysis in Mentally Deficient Children, J. Abnorm. & Social Psychol. **34**:37-62, 1939.

Strauss, A., and Werner, H.: Finger Agnosia in Children, Am. J. Psychiat. **95**:1215-1225 (March) 1939.

Case Reports

ADHESIVE SPINAL ARACHNOIDITIS AS A CAUSE OF INTRAMEDULLARY CAVITATION

Comparison with Syringomyelia

ALBERT J. LUBIN, M.D., SAN FRANCISCO

Adhesive spinal arachnoiditis may cause profound changes within the spinal cord. These changes include cavitation. Hense the condition may be confused not only clinically but pathologically with syringomyelia. Only a few authors (Schwarz,[1] Harbitz and Lossius,[2] Yasuda [3] and Mackay [4]) have discussed cavitation from this cause. Schwarz in 1897 demonstrated preparations in a case of "syphilitic meningomyelitis" with cavitation in the cord. His description corresponds closely with present concepts of adhesive spinal arachnoiditis. Yasuda presented 3 cases of "arachnopathia fibrosa cystica proliferans" from Foerster's clinic; in each there were features suggesting syringomyelia. Mackay recently reported a case of arachnoiditis with cavitation found at autopsy and concluded that "future studies of 'syringomyelia' must take this into account." The only detailed pathologic study in the American literature besides that of Mackay is that of Grinker,[5] in whose case there were but few intramedullary changes.

In a previous paper [6] the belief was expressed that syringomyelia, sui generis, is a developmental anomaly caused by imperfect closure of the central canal with resultant cell rests later undergoing gliosis; cavitation results from insufficient blood supply to the gliotic tissue. Such cavitation must be distinguished from cavitation resulting from other conditions, such as adhesive spinal arachnoiditis, in which the same factors of insufficient blood supply and subsequent ischemic necrosis are present. Other causes of intramedullary cavitation include embolus or thrombosis of the spinal arteries, hematomyelia, tumors of the intra-

From the Division of Neuropsychiatry of the Stanford University School of Medicine.

1. Schwarz, E.: Präparate von einem Falle syphilitischer Myelomeningitis mit Höhlenbildung im Rückenmarke und besonderen degenerativen Veränderungen der Neuroglia, Wien. klin. Wchnschr. **10**:177, 1897.

2. Harbitz, F., and Lossius, I.: Extramedullary Tumor; Arachnitis Fibrosa Cystica et Ossificans; Gliosis of the Medulla, Acta psychiat. et neurol. **4**:51, 1929.

3. Yasuda, T.: Zur Frage der Arachnopathia fibrosa cystica proliferans, Deutsche Ztschr. f. Nervenh. **143**:61, 1937.

4. Mackay, R. P.: Chronic Adhesive Spinal Arachnoiditis: A Clinical and Pathologic Study, J. A. M. A. **112**:802 (March 4) 1939.

5. Grinker, R. R.: Chronic Arachno-Perineuritis with the Syndrome of Froin: Report of a Case with a Discussion of Pseudotumor Spinalis, J. Nerv. & Ment. Dis. **64**:616, 1926.

6. Tamaki, K., and Lubin, A. J.: Pathogenesis of Syringomyelia: Case Illustrating the Process of Cavity Formation from Embryonic Cell Rests, Arch. Neurol. & Psychiat. **40**:748 (Oct.) 1938.

medullary portion of the cord, myelitis, meningomyelitis, trauma and experimental procedures.[7]

The present case of adhesive spinal arachnoiditis demonstrates marked intramedullary changes and cavitation. The relation between this cavitation and that associated with syringomyelia will be discussed.

REPORT OF A CASE

Weakness and atrophy of the arms and sensory disturbances for two years; Babinski sign and increased deep reflexes in the legs; spinal block; operation; death; widespread inflammation of the arachnoid and cyst formation; dense leptomeningeal fibrosis in the cervical region, with intramedullary vascular thickening, necrosis and cavitation.

History.—C. N., a Dutch sailor, aged 36, entered the outpatient clinic complaining of loss of strength in the arms for the preceding eight months. He first noticed weakness of his left arm, followed in three months by fibrillary twitching of the left biceps and a feeling of numbness in the same extremity. Five months after the onset, weakness of the right arm developed without fibrillations or sensory disturbances.

There was a history of a chancre ten years previously, which had been treated with eight injections of arsphenamine. He was otherwise well until the present illness. The family history was not remarkable.

Examination.—The patient was emaciated. Marked atrophy and loss of power of the left shoulder muscles, the biceps, the flexor muscles of the wrist and the interosseus muscles were present. The right shoulder muscles and biceps were atrophied to a lesser extent. There was a coarse tremor of both hands, with lack of coordination of the left. The biceps and radial reflexes were absent on the left, and the biceps reflex was diminished on the right. The triceps reflexes were sluggish bilaterally. The superficial abdominal reflexes were absent. Pain and temperature sensation was absent over the entire left arm and hand and the back of the right shoulder. Tactile sensibility was diminished over the posterior aspect of the left forearm and hand. The Romberg sign was positive.

The results of routine blood count and urinalysis were not remarkable. The Wassermann reaction of the blood and of the cerebrospinal fluid was negative. There was no increase of cells or protein in the spinal fluid. The Lange test of the lumbar fluid yielded a curve of 4454453211, and that of the cisternal fluid, a curve of 324321000.

Course.—Eighteen months later the patient entered the neuropsychiatric ward because of increased weakness. The atrophies and sensory disturbances had progressed. Signs of involvement of the pyramidal tract had appeared in both lower extremities, with a Babinski sign and increased knee and ankle jerks. Combined cisternal and lumbar punctures revealed complete spinal block. After constriction

---

7. Philippe, C., and Oberthür, J.: Classification des cavités pathologiques intra-médullaries: I. Syringomyélie vraie; forme cavitaire et forme pachyméningitique; II. Pseudosyringomyélies (hydromyélie; hematomyélie; cavités vasculaires; cavités traumatiques), Rev. neurol. **8**:171, 1900. Davison, C., and Keschner, M.: Myelitic and Myelopathic Lesions: VI. Cases with Marked Circulatory Interference and a Picture of Syringomyelia, Arch. Neurol. & Psychiat. **30**:1074 (Nov.) 1933. Tauber, E. S., and Langworthy, O. R.: A Study of Syringomyelia and Formation of Cavities in the Spinal Cord, J. Nerv. & Ment. Dis. **81**:245, 1935.

of the internal jugular vein the cisternal pressure rose from 85 mm. to 300 mm., while the lumbar pressure (of 100 mm.) did not increase.

Operation.—Laminectomy of the third, fourth and fifth cervical vertebrae was performed. An intramedullary cavity was found at the fourth cervical segment. The patient died eight days later with terminal bronchopneumonia.

Necropsy.—Aside from extensive bilateral bronchopneumonia, the essential findings were confined to the central nervous system, which was removed and fixed in diluted solution of formaldehyde U. S. P. (1:10).

Macroscopic Examination: The brain was grossly normal. The spinal dura was somewhat thickened in the cervical region, especially posteriorly. Beneath the surgical sutures in the dura of the fourth cervical segment was a short midline incision extending into an intramedullary cavity. There were adhesions between the dura and the arachnoid from the third to the sixth cervical segment. The arachnoid was markedly hyperplastic and adherent to the cord from the third to the seventh cervical segment. The cord was compressed in the same area. The anterior spinal vessels were indistinct from the fourth cervical segment to the midthoracic region.

Microscopic Examination: Pyroxylin sections were made from every segment of the cord and from the cortex, midbrain and medulla. The following stains were used: hematoxylin and eosin, the phosphotungstic acid–hematoxylin stain, Van Gieson's stain, the Pal-Weigert stain and Hortega's stain.

Changes in the arachnoid were noted throughout the entire cerebrospinal axis, although these were slight below the thoracic region. These changes varied from a marked cellular and fibroblastic proliferation (in the thoracic segments and to a lesser extent in the brain) to dense, adherent constrictive fibrosis (in the midcervical region, where the pia was also thickened). The fibrosis was greatest at the fourth cervical segment, where destruction of the spinal cord and cavitation were most marked and where the subarachnoid space was obliterated.

The cellular elements in the arachnoid consisted of lymphocytes, plasma cells and gitter cells in a loose network of fibroblasts. There were several arachnoidal cysts in the thoracic region, where this cellular type of lesion predominated, lined by fibroblasts or arachnoidal cells. In the pia there were numerous perivascular infiltrations of lymphocytes and plasma cells. The older fibrotic lesions in the arachnoid consisted mainly of collagenous fibers. In several places connective tissue fibers were arranged in tumors resembling meningiomas. Psammoma bodies occurred frequently in the arachnoid. Nerve roots were entangled in the hyperplastic arachnoid of the midcervical region.

There was an increase of connective tissue in the dura of the cervical region, but this was not as marked or as extensive as was the hyperplasia of the arachnoid (in contrast to the changes associated with cervical hypertrophic pachymeningitis).

Cavity formation was present in the spinal cord between the second cervical and the first thoracic segment. The most cephalad cavitation began in the apex of the left posterior gray column of the second cervical segment and extended diagonally toward the dorsolateral fasciculus (Lissauer), growing larger and encroaching into the fasciculus cuneatus in the third cervical segment. In the fourth cervical segment this cavity became larger and irregular. There were three smaller cavities on the right side, one crossing at the posterior commissure and involving the central canal for a short distance and another crossing the posterior median septum and joining the large cavity on the left. In the lower part of the fourth cervical segment the larger cavities disappeared, and numerous smaller, slitlike cavities remained. These

merged into two cavities in the fifth cervical segment: one with a regular outline in the left fasciculus cuneatus and the other, irregular, on the right side of the cord. In the sixth cervical segment there was evidence of an old hemorrhage into one of the cavities. In the seventh cervical segment there was only one cavity, lying above and to the left of the central canal, becoming smaller and disappearing in the first thoracic segment.

Many of the cavities had no well defined borders but lay in the center of necrotic tissue. Other cavities had regular borders lined by fibroblasts. In a few places the borders consisted of an acellular homogeneous material resembling the "areas of homogenization" described by Hassin [8] as occurring with syringomyelia. In the fourth cervical segment a cavity was partially lined by ependyma for a short distance owing to encroachment on the central canal.

The cord was not involved below the first thoracic segment except for the previously noted meningeal changes and a mild *Rand-degeneration.* There were areas of necrosis between the second cervical and the first thoracic segment. Throughout the cervical portion of the cord there were degenerative changes in cells of the anterior horn, consisting of central chromatolysis and eccentric nuclei without satellitosis or neuronophagia. Nerve cells were practically absent in the fourth cervical segment, where the cord had undergone the greatest distortion. The posterior columns, particularly the fasciculus gracilis, exhibited marked myelin degeneration from the sixth cervical segment to the medulla (ascending degeneration), as shown by the Pal-Weigert method.

In the acutely necrotic areas there was no evidence of repair. In other areas some repair had occurred, with proliferation of fibroblasts and a moderate increase in glia. *Gemästete* cells were present in these areas. Immediately surrounding cavities, fibroblastic proliferation was prominent, while the glial changes were more evident peripherally. Many gitter cells were present, especially near cavities. The central canal was normal except in the fourth cervical segment, as has been noted.

Thickening of the walls of the blood vessels was prominent throughout the cervical portion of the cord and was most severe at the fourth cervical segment, the level of greatest distortion. The adventitia, the media and, to a lesser extent, the intima were involved. Some vessels were almost completely occluded. There also was a marked increase in the number of blood vessels, especially about areas of softening and cavitation.

Comment.—As in many others reported, the etiologic factor in this case is not clear. The role of syphilis is questionable despite the history of a chancre ten years previously, in view of the fact that the Wassermann reaction of both the blood and the cerebrospinal fluid was negative. Although perivascular infiltration of lymphocytes and plasma cells is commonly observed in syphilitic lesions, such an observation is not pathognomonic. Mackay,[4] whose cases resembled this one in many respects, expressed the opinion that the tissue reactions in patients with adhesive spinal arachnoiditis are more or less stereotyped, regardless of the cause.

There are said to be numerous causes of spinal arachnoiditis, but in many cases no definite cause is found. In some cases the condition follows attacks of acute meningococcic meningitis. Other infectious diseases reported as etiologic factors include lymphocytic choriomenin-

8. Hassin, G. B.: A Contribution to the Histopathology and Histogenesis of Syringomyelia, Arch. Neurol. & Psychiat. **3**:130 (Feb.) 1920.

gitis,[9] syphilis,[10] tuberculosis [11] and gonorrhea.[12] Trauma has been emphasized as an important cause.[13] Mauss and Krüger [14] reported 23 cases in which the disease was due to war injuries of the vertebral column.

GENERAL COMMENT

The several stages of a process marked by inflammatory changes in the arachnoid and subsequent development of intramedullary softening and cavitation are illustrated in this case.

The changes in the arachnoid are progressive but for convenience may be described as: (*a*) an early, proliferative stage and (*b*) a later, constrictive stage. In the present case various portions of the cord showed widely different stages of the process. The proliferative stage (fig. 1), as observed in the thoracic segments of the spinal cord, is characterized by: (1) the presence of numerous lymphocytes, plasma cells and fat-laden gitter cells (fig. 2) in a loose stroma of fibrous tissue; (2) the formation of arachnoidal cysts (fig. 3) lined with fibroblasts, and (3) perivascular infiltration of inflammatory cells in the pia (fig. 4). In this stage there are no intramedullary changes. The constrictive stage (fig. 5), as observed in the cervical segments, is characterized by: (1) dense fibrosis, with a paucity of cellular elements and disappearance of most of the cysts; (2) adherence of the leptomeninges to the cord, with obliteration of the subarachnoid space, and (3) thickening of the walls of the pial blood vessels and narrowing of their lumens.

With the dense fibrosis and vascular thickening in the leptomeninges, intramedullary changes occur (fig. 6). The thickening of the vessel walls extends into the cord (fig. 7), causing diminution of the blood supply; areas of softening appear, finally leading to cavitation (fig. 8). In a later stage the cavities are lined with connective tissue, and a moderate proliferation in glia occurs in the surrounding tissue.

The cavitation in cases of adhesive spinal arachnoiditis should be compared (fig. 9) with that in cases of true syringomyelia (*syringomyélie vraie* of Philippe and Oberthür). In both conditions there is the factor of deficient intramedullary blood supply, but the pathologic changes preceding this deficiency vary widely in the two diseases. True syringomyelia is due to imperfect development of the central canal by the primitive medullary epithelium,[6] with the resultant cell rests, com-

9. Barker, L. F., and Ford, F. R.: Chronic Arachnoiditis Obliterating the Spinal Subarachnoid Space, J. A. M. A. **109**:785 (Sept. 4) 1937.

10. Clarke, N. E.: Loculated Meningitis with the Syndrome of Froin in the Spinal Fluid, Arch. Neurol. & Psychiat. **12**:173 (Aug.) 1924.

11. Brouwer, B.: Ueber Arachnoiditis adhaesiva circumscripta, Deutsche Ztschr. f. Nervenh. **117-119**:38, 1931.

12. Horsley, V.: Chronic Spinal Meningitis: Its Differential Diagnosis and Surgical Treatment, Brit. M. J. **1**:513, 1909.

13. Elkington, J. St. C.: Meningitis Serosa Circumscripta Spinalis (Spinal Arachnoiditis), Brain **59**:181, 1936.

14. Mauss, T., and Krüger, H.: Ueber die unter dem Bilde der Meningitis serosa circumscripta verlaufenden Kriegsschädigungen des Rückenmarkes und ihr operative Behandlung, Deutsche Ztschr. f. Nervenh. **62**:1, 1918.

Fig. 1.—Proliferative stage in the arachnoid of the sixth thoracic segment. The numerous inflammatory cells and macrophages lie in a stroma of fibroblasts. Hematoxylin and eosin stain.

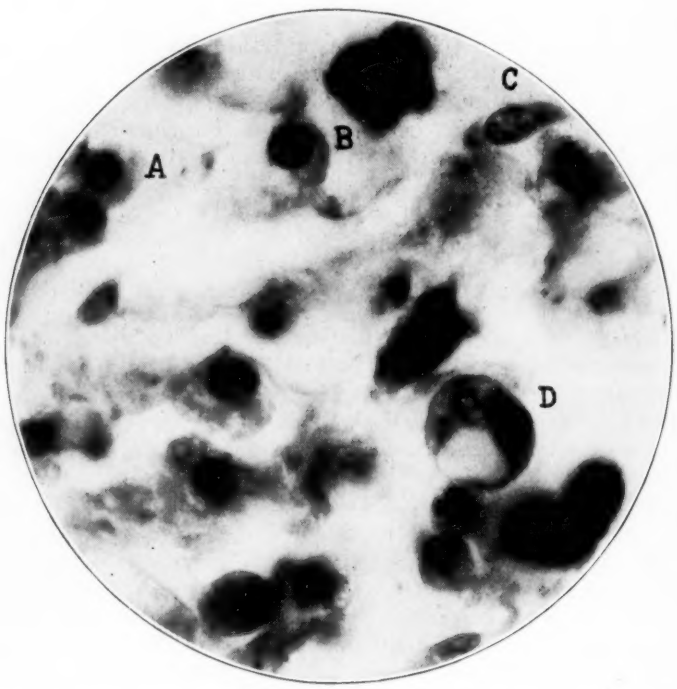


Fig. 2.—Cellular detail of the section in figure 1, showing a lymphocyte (*A*), a plasma cell (*B*), a fibroblast (*C*) and a gitter cell (*D*). Hematoxylin and eosin stain.

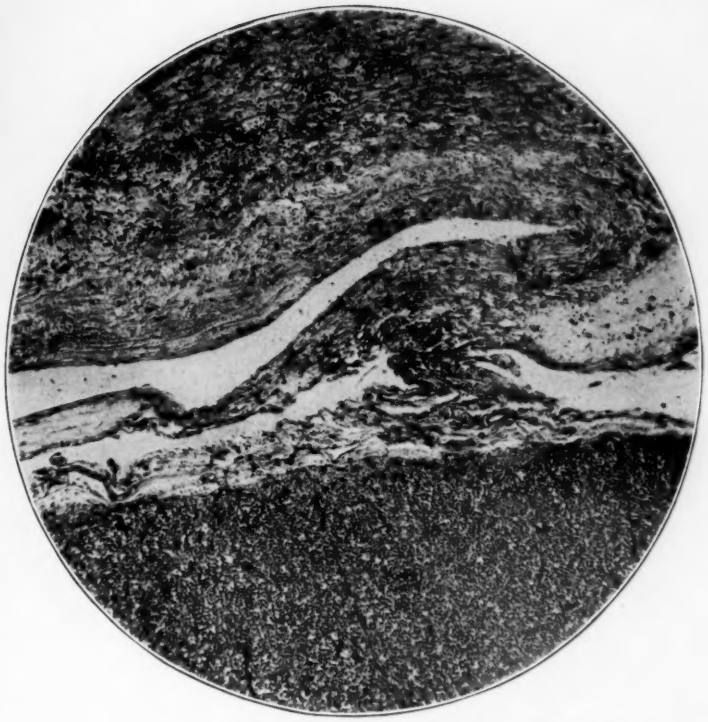


Fig. 3.—Leptomeninges of the ninth thoracic segment with an arachnoidal cyst lined with fibroblasts. Hematoxylin and eosin stain.

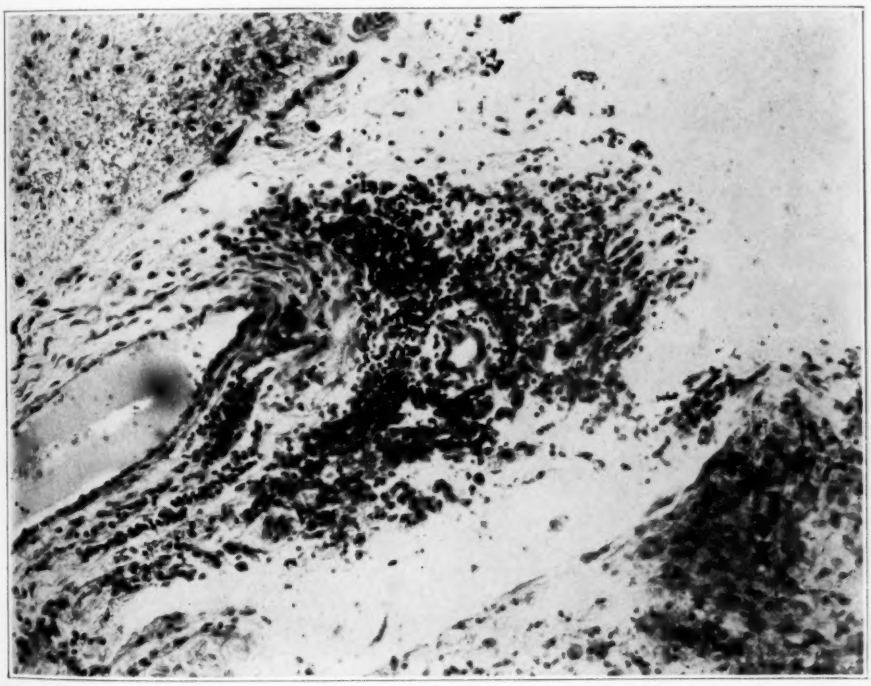


Fig. 4.—A pial artery with perivascular cuffing. Fifth cervical segment; hematoxylin and eosin stain.

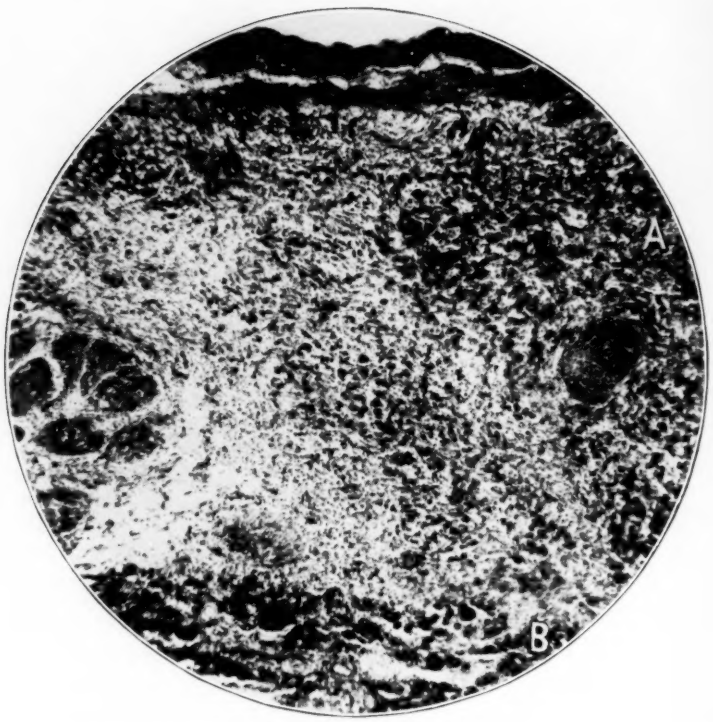


Fig. 5.—Fibrous constrictive stage, with dense fibrosis of the arachnoid (*A*) and obliteration of the subarachnoid space (*B*). Phosphotungstic acid–hematoxylin stain.

Fig. 6.—Spinal cord of the fourth cervical segment, showing the constricting pia-arachnoid, obliteration of the subarachnoid space and intramedullary cavity formation. Phosphotungstic acid–hematoxylin stain.

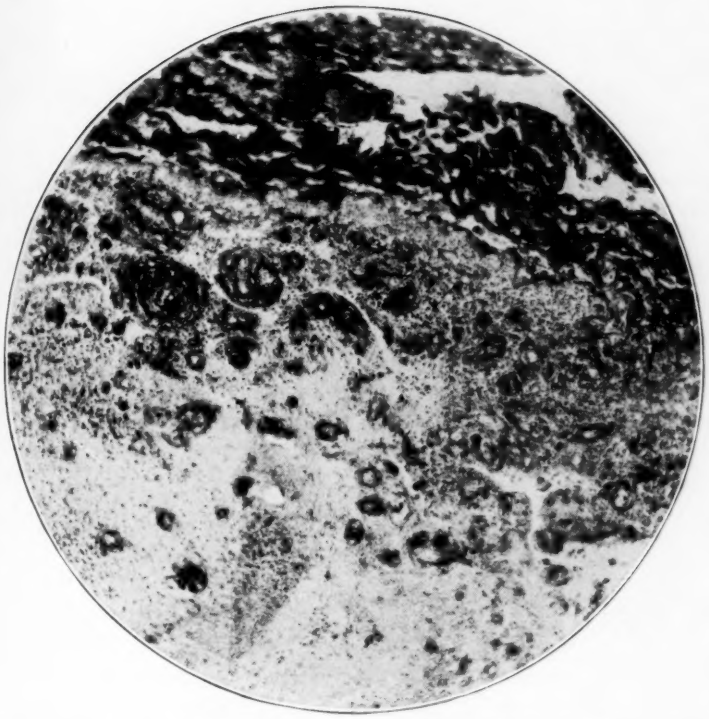


Fig. 7.—Marked thickening and increase in number of the blood vessels of the fifth cervical segment. Phosphotungstic acid–hematoxylin stain.

Fig. 8.—Intramedullary cavity formation. The central canal (*A*) is normal. Eighth cervical segment; hematoxylin and eosin stain.

posed of ependymal spongioblasts, causing marked gliosis in the surrounding tissue. Thickening of the vessel walls and meninges is secondary to this developmental anomaly. The deficient blood supply leads to intramedullary necrosis and cavitation, just as in cases of adhesive spinal arachnoiditis. The characteristics that distinguish the cavitation associated with adhesive spinal arachnoiditis from that observed with syringomyelia (see table) are:

1. With the former the process is primarily in the pia-arachnoid, and arachnoidal changes may be distinguished in regions remote from any intramedullary abnormality. In syringomyelia the arachnoid is involved secondarily,[15] and arachnoidal thickening occurs only near regions of intramedullary changes.

2. In the presence of adhesive spinal arachnoiditis inflammatory signs are present, such as infiltration of lymphocytes and plasma cells

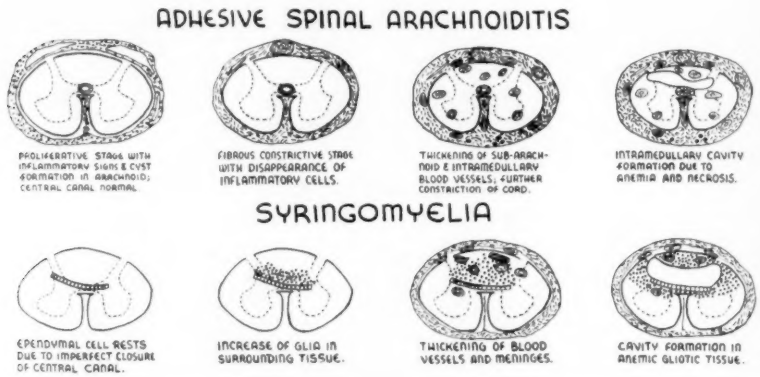

ADHESIVE SPINAL ARACHNOIDITIS
PROLIFERATIVE STAGE WITH INFLAMMATORY SIGNS & CYST FORMATION IN ARACHNOID; CENTRAL CANAL NORMAL
FIBROUS CONSTRICTIVE STAGE WITH DISAPPEARANCE OF INFLAMMATORY CELLS.
THICKENING OF SUB-ARACHNOID & INTRAMEDULLARY BLOOD VESSELS; FURTHER CONSTRICTION OF CORD.
INTRAMEDULLARY CAVITY FORMATION DUE TO ANEMIA AND NECROSIS.
SYRINGOMYELIA
EPENDYMAL CELL RESTS DUE TO IMPERFECT CLOSURE OF CENTRAL CANAL.
INCREASE OF GLIA IN SURROUNDING TISSUE.
THICKENING OF BLOOD VESSELS AND MENINGES.
CAVITY FORMATION IN ANEMIC GLIOTIC TISSUE.

Fig. 9.—Diagrammatic sketch comparing the pathogenesis of intramedullary cavity formation in cases of adhesive spinal arachnoiditis and in cases of syringomyelia.

in the arachnoid and perivascular cuffing in the pia. Such inflammatory signs are absent in cases of syringomyelia.

3. Arachnoidal cysts frequently occur in cases of adhesive spinal arachnoiditis and probably are never found in association with syringomyelia.

4. Obliteration of the subarachnoid space is found in an early stage of adhesive spinal arachnoiditis but occurs late, if at all, in the course of syringomyelia.

5. Glial proliferation in a patient with adhesive spinal arachnoiditis may be absent and in any case is less pronounced than in the presence of syringomyelia, in which it is an essential part of the process.

15. Alajouanine, T.; Hornet, T.; Thurel, R., and André, R.: Le feutrage arachnoïdien postérieur dans la syringomyélie (sa place dans la pathologie des leptoméninges), Rev. neurol. **64**:91, 1935.

6. Although ependymal abnormalities occur rather frequently in otherwise normal cords,[16] they are not an essential feature of adhesive spinal arachnoiditis, while in cases of syringomyelia such abnormalities are a sine qua non. Likewise, other congenital anomalies, such as spina bifida and cervical rib, are frequently associated with syringomyelia,[16a] but are presumably rare with spinal arachnoiditis.

7. Cavitation in a case of adhesive spinal arachnoiditis may occur in any portion of the cord without any constant relation to the ependyma of the central canal, and the cavities are frequently lined with connective tissue and infrequently with ependyma. In nearly all cases of syringomyelia part of the cavitation is lined with ependyma, as Schlesinger [17] pointed out many years ago.

Comparison of Adhesive Spinal Arachnoiditis and Syringomyelia

	Adhesive Spinal Arachnoiditis	Syringomyelia
Cause	Infection; trauma; unknown	Developmental anomaly; other congenital anomalies often present (spina bifida, etc.)
Pathogenesis	Leptomeningeal inflammation; fibrosis; pial vascular thickening; intramedullary vascular thickening; ischemic necrosis; cavitation	Ependymal cell rests; gliosis; vascular thickening; ischemic necrosis; cavitation
Pia-arachnoid	Primary site of process	Involvement secondary to intramedullary changes
Inflammatory signs	Prominent	Absent
Subarachnoid space	Obliterated relatively early	Obliterated late, if at all
Vascular thickening	Marked	Less marked
Arachnoidal cysts	Common	Absent
Cord	1. Involvement secondary to leptomeningeal changes	1. Primary site of process
	2. Posterior columns usually affected first	2. Commissural fibers affected first
Cavitation	No constant relationship to ependyma	Partly lined by ependyma
Gliosis	Usually moderate; may be absent	Marked
Central canal	Normal	Malformed
Vascular thickening	Present	Present (earlier ?)

8. In the presence of adhesive spinal arachnoiditis the posterior columns are usually involved, as with any condition causing diffuse compression of the spinal cord, possibly because these structures are

16. Rolly: Ueber periependymäre Wucherung, Kanalbildung und abnorme Entwicklungsvorgänge am kindlichen Rückenmarkskanal, Deutsche Ztschr. f. Nervenh. **21**:355, 1902. Cornil, L., and Mosinger, M.: Sur les processus prolifératifs de l'épendyme médullaire (rapports avec les tumeurs intramédullaires et la syringomyélie), Rev. neurol. **1**:749, 1933.

16a. Haenel, H.: Syringomyelie, in Bumke, O., and Foerster, O.: Handbuch der Neurologie, Berlin, Julius Springer, 1911, vol. 2, p. 572. Bremer, F. W.: Klinische Untersuchungen zur Aetiologie der Syringomyelie, der „Status dysraphicus", Deutsche Ztschr. f. Nervenh. **95**:1, 1926.

17. Schlesinger, H.: Die Syringomyelie, ed. 2, Leipzig, Franz Deuticke, 1902.

comparatively young in phylogenetic development.[18] In syringomyelia the commissural fibers are the earliest to be involved, because of the central origin of the process.

SUMMARY

A comparative study of the pathogenesis of intramedullary cavity formation in adhesive spinal arachnoiditis and syringomyelia is presented. The several stages of the pathogenesis of adhesive spinal arachnoiditis are:

1. An early proliferative stage involving the arachnoid with numerous inflammatory cellular elements.

2. A later, constrictive stage with dense fibrosis of the leptomeninges and obliteration of the subarachnoid space.

3. Thickening of vascular walls in both the pia and the spinal cord, leading to ischemic necrosis and cavitation.

In contrast, an anomaly in development may be demonstrated in cases of syringomyelia:

1. Ependymal cell rests due to imperfect closure of the central canal lead to gliosis in the surrounding tissue.

2. Thickening of the vascular walls and of the leptomeninges are secondary to the intramedullary gliosis; ischemic necrosis and cavitation follow.

CONCLUSION

Intramedullary cavitation may be due to a variety of causes and in itself does not justify the diagnosis of syringomyelia. Adhesive spinal arachnoiditis is one of these causes. It may be differentiated from true syringomyelia by (1) demonstration of the primary inflammatory leptomeningeal involvement with arachnoidal cyst formation and (2) the absence of essential ependymal abnormalities.

Dr. K. Tamaki and Dr. L. J. Whitsell assisted in the preparation of the paper.

Dr. Walter F. Schaller furnished the pathologic material.

18. Brouwer, B.: The Significance of Phylogenetic and Ontogenetic Studies for the Neuropathologist, J. Nerv. & Ment. Dis. **51**:113, 1920.

HUMAN BEHAVIOR AFTER EXTENSIVE BILATERAL REMOVAL FROM THE FRONTAL LOBES

D. O. Hebb, Ph.D., and Wilder Penfield, M.D., D.Sc., Montreal, Canada

At rare intervals chance presents to a neurosurgeon a lesion of the brain demanding treatment that would satisfy the exacting requirements of an extirpation experiment. This was true of the case we are about to record. Psychologic studies of the patient were made before, during and after an extensive bilateral frontal lobectomy, without yielding evidence of postoperative deterioration such as might have been expected from earlier examinations, and particularly from the case studied in detail by Brickner.[1] It becomes evident that human behavior and mental activity may be more greatly impaired by the positive action of an abnormal area of brain than by the negative effect of its complete absence,[2] and the case reported here presents a new opportunity for study of the functions of the frontal lobes.

REPORT OF A CASE

History.—K. M., a man aged 27, who was right handed, came to the clinic in April 1938, seeking relief from post-traumatic epilepsy. In 1928, at the age of 16, he had been struck on the forehead by an overhead carrier in a sawmill and rendered immediately unconscious. He remained in this condition for ten days. At the time of the accident the left orbit was pushed downward and the left eye extruded somewhat. A depressed fracture of the frontal bone, rather greater on the left, is said to have been observed at operation; some fragments of bone were elevated, and the scalp was sutured.

After recovery from the immediate effects of the accident there were frequent frontal headaches. Six months after the accident major epileptic seizures began, and continued with increasing frequency. During the month preceding admission to the Montreal Neurological Institute there were six such attacks. Each seizure began with an aura which the patient described as a smothering sensation originating in the epigastrium and moving up to the throat. This was occasionally accompanied by a complicated visual and auditory hallucination. The person

---

From the Montreal Neurological Institute and the Department of Neurology and Neurosurgery, McGill University.

1. Brickner, R. M.: An Interpretation of Frontal Lobe Function Based upon the Study of a Case of Partial Bilateral Frontal Lobectomy, A. Research Nerv. & Ment. Dis., Proc. (1932) **13**:259-351, 1934; The Intellectual Functions of the Frontal Lobes: A Study Based upon Observation of a Man After Partial Bilateral Frontal Lobectomy, New York, The Macmillan Company, 1936; Bilateral Frontal Lobectomy: Follow-Up Report of a Case, Arch. Neurol. & Psychiat. **41**:580-583 (March) 1939.

2. (*a*) Jefferson, G.: Removal of Right or Left Frontal Lobes in Man, Brit. M. J. **2**:199-206, 1937; (*b*) Frontallappenresektion: Ein Bericht über 13 Fälle, Helvet. med. acta **5**:777-782, 1938. (*c*) Hebb, D. O.: Intelligence in Man After Large Removals of Cerebral Tissue: Report of Four Left Frontal Lobe Cases, J. Gen. Psychol. **21**:73-87, 1939.

who had last spoken to the patient might appear in front of him and continue to talk as he or she had done when last seen, although the patient could not understand the words. Perhaps it would be better to call this a memory rather than a true hallucination.

Ordinarily the aura lasted from one to two seconds. The patient then cried loudly, fell to the floor in a tonic-clonic seizure, bit his tongue and voided. After a few minutes he rose and walked about unsteadily in an automatic state. At such times he might strike any object in his path. He thrust his fist through a door on several occasions, and would violently resist any attempt of others to restrain him. Between attacks the patient had become a behavior problem—irresponsible, childishly stubborn, restless and forgetful. Apparently, the abnormality of behavior varied in degree, but was not related directly to the overt

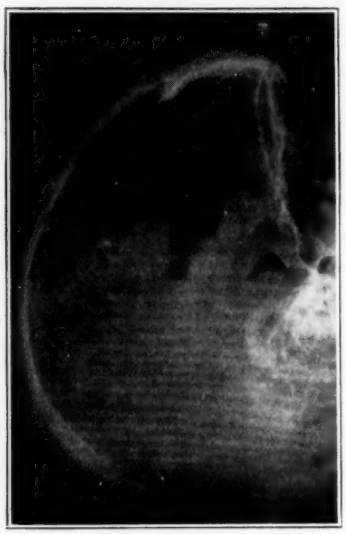


Fig. 1.—Pneumoencephalogram before operation, showing depression of the skull, superficial cysts and enlargement of portion 1 of the lateral ventricles. The film was taken with the brow up.

attacks. The only abnormalities of which the patient himself was aware were the attacks, deficiency of memory and inability to concentrate.

Examination.—The physical condition was essentially normal except for a frontal scar. The results of psychologic tests before operation will be described later, under the heading of "Psychologic Data." Pneumoencephalograms showed that the cerebral ventricles were of normal size and shape, except that the anterior tips (portion 1) of both ventricles were enlarged slightly (fig. 1). Superficial cysts were demonstrated beneath the line of fracture over both frontal poles. The large depression of the skull may be seen in figure 1.

Electroencephalographic study by Dr. Herbert Jasper showed bursts of epileptiform activity from both frontal regions, possibly more from the right than from the left. There were 3 per second waves of large amplitude and random spike activity.

Comment.—Because of the hopeless outlook for the patient's leading a useful life, it was decided to remove the injured areas of brain, with the hope of leaving only convolutions capable of normal function. The removal was carried out according to principles already described.[3]

Operation.—Osteoplastic craniotomy was carried out in the left and right frontal regions, with the use of local anesthesia. There was a partial defect in the dura near the fracture, and here the bone was pitted. The longitudinal sinus was thrombosed anteriorly. The dura was dissected free from the adherent brain, and the anterior 6 cm. of the falx was cut and reflected. This exposed a large cicatrix in both frontal lobes, made up of tough, gelatinoid material which had been densely attached to the dura (fig. 2). The scar, which contained numerous small cysts,

Fig. 2.—Photograph taken during operation, before removal of scar tissue. The cutting sutures may be seen in place, about a centimeter posterior to the scar. The reflected anterior part of the falx is in the upper left portion of the picture.

collapsed after it was dissected free from the dura. The alteration and destruction involved both frontal poles back to and including the tips of the anterior ventricular horns.

Electrical stimulation was without positive result and produced no seizure. Electroencephalographic records were taken from the exposed portion of the brain and the scar. Electrical activity was found, of course, in the brain at the periphery of the scar, but not in the scar tissue itself.

---

3. Penfield, W.: Epilepsy and Surgical Therapy, Arch. Neurol. & Psychiat. **36**:449-484 (Sept.) 1936.

On continuing the surgical procedure, the frontal pole was removed on each side back to the level of the normal convolutions. The removal was begun with cutting sutures, as seen in figure 2, and was completed with suction, care being taken to leave only tissue which seemed normal and well vascularized. From 0.5 to 1 cm. of comparatively normal cerebral tissue was thus removed beyond the scar. After removal was completed, inspection showed that both ventricles had been transected, a little more of the right than of the left ventricle being exposed. On the left side the whole orbital plate was exposed, back to the edge of the lesser wing of the sphenoid bone. On the right the line of removal was about 0.5 cm. anterior to this. Laterally the line of removal on each side was from 1 to 1.5 cm. anterior to the level of removal in the midline (fig. 3).

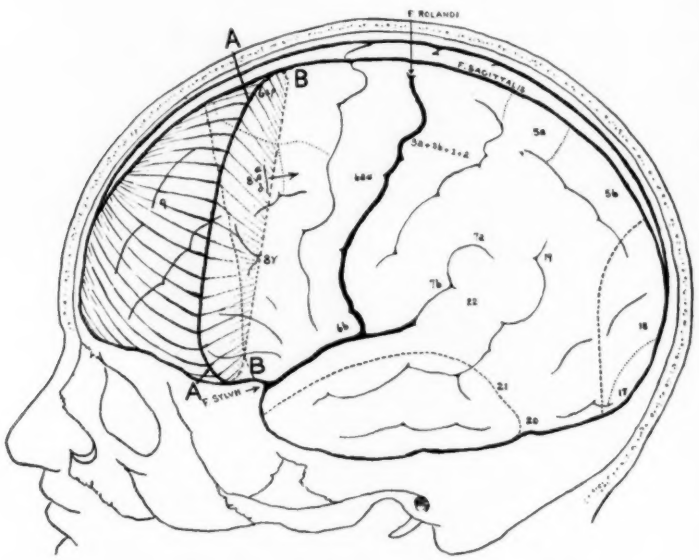


Fig. 3.—Diagram showing extent of removal as seen laterally, from the left. This is reproduced from a sketch made at operation, by using a previously prepared life-size diagram of the brain and skull and transferring to it actual anteroposterior measurements of the defect. The patient's skull was apparently slightly smaller than the diagram, making the defect appear in the diagram somewhat smaller (in relation to the rest of the brain) than it should have been. The curved solid line, *AA*, represents the line of excision laterally; the broken line, *BB*, the line of excision medially. These should be slightly farther back (see fig. 4).

Both anterior cerebral arteries were exposed, and the removal was carried out about 2 cm. posterior to the forward curving course of these arteries (fig. 4), the corpus callosum being much atrophied anteriorly. The anterior cerebral arteries continued to pulsate at the close of the dissection. The olfactory bulbs were exposed, but were left intact (fig. 4). The dura was then repaired, and the bone flaps were replaced and wired in place.

The patient was conscious and cooperative throughout. After the surgical removal had been completed it was desired to put the patient to sleep. The anesthetist therefore introduced a catheter into the rectum in order to give him a soporific dose of avertin with amylene hydrate. During the introduction of the tube the patient made inappropriately facetious remarks, but there was no other abnormality of behavior throughout the course of the operation.

Convalescence.—The suggestion of facetiousness which appeared at the conclusion of the operation increased next day, and then disappeared for two or three days. There was at first no other evidence of intracranial disturbance,

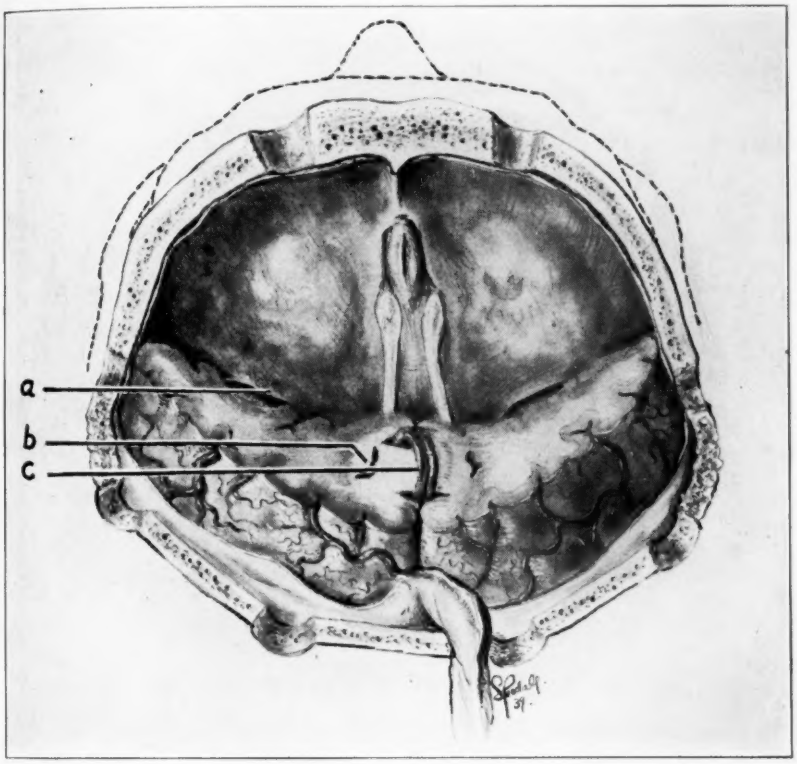


Fig. 4.—Sketch of the operative defect as seen from above with the patient's brow up. Here, *a* indicates the partly exposed posterior margin of the lesser wing of the sphenoid bone; *b*, the transected ventricle, and *c*, the anterior cerebral arteries curving forward around the corpus callosum.

except for frontal headache, which gradually became severe. On the sixth day, however, the patient became irrational and later almost comatose; the left pupil was dilated and fixed, and the left eye turned somewhat outward. Fluid removed by puncture from the frontal defect was deep orange. After the first week it gradually became lemon colored and remained so until the patient was discharged. There was obvious communication between the area of operation and the lumbar

sac, and the total protein content of the cerebrospinal fluid was high, at one time reaching 675 mg. per hundred cubic centimeters.

On the tenth day after operation the patient was again responsive, but was disoriented, irrational and slightly facetious and used obscene language. The facetiousness was not extreme and was often hard to distinguish from the patient's usual jocular manner and conversation, but the nurses in attendance stated that it lasted until about the fortieth day after operation.

Three grains (0.195 Gm.) of phenobarbital daily was given for the first thirty days; thereafter the dose was 1 grain (0.065 Gm.) daily. When the patient was discharged on the fifty-fifth day, the resident, Dr. Lister Reid, made the following note: "The patient has now a pleasant personality. He is no longer facetious or vulgar . . . but is considerate of the other patients and has acquired a pleasant sense of humor."

Fig. 5.—Photograph of K. M. fifteen months after operation.

Five months after operation the total protein level of the spinal fluid was still elevated to 140 mg. per hundred cubic centimeters, although the fluid had become completely colorless. Six months and fourteen months after operation the patient, on his own initiative, temporarily ceased to take 1 grain of phenobarbital daily. On both occasions he had an epileptic attack, in which he bit his tongue. Otherwise, he had been free from seizures since operation, and his personality was described by relatives as completely changed for the better, as will be described.

Fifteen months after operation the patient returned to the Montreal Neurological Institute for clinical and psychologic examination (fig. 5). His physical condition was essentially the same as on discharge. He was still taking 1 grain of phenobarbital daily and had been working half time on his father's farm. He appeared alert and satisfied with the results of operation. The spinal fluid was found to be normal except for an increase in protein. Pneumoencephalograms revealed that the ventricles were of normal size and shape and that they

communicated with large frontal spaces, as shown in an earlier postoperative encephalogram (fig. 6).

Two electroencephalographic examinations were made. On one occasion no abnormality of electrical potentials was discovered. On the other the following report was made: "Bursts of 3 per second waves were no longer present, and epileptiform spikes were no longer obtained in the right frontal region. On the left side no abnormal activity was obtained from the preoperative focus, but there was suggestive evidence of a mildly active focus of epileptiform activity in the posterolateral frontal region. Here, there occurred occasional random spikes."

As far as could be determined from the electrical study, the pathologic activity originating in both frontal regions before operation had almost entirely disappeared. Occasional random spike-shaped waves near an area of removal is a frequent finding in cases of this kind, the significance of which is not yet clearly understood.

ANATOMIC ANALYSIS

The line of removal in each frontal lobe was estimated at the time of operation to be equidistant between the point where the anterior tip of the lobe should be

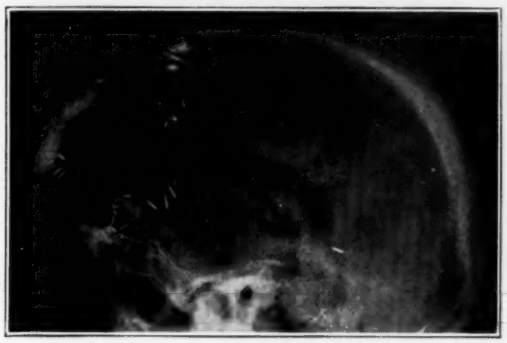


Fig. 6.—Encephalogram one month after operation, showing unenlarged ventricles communicating with the frontal defect. The film was taken with the side of the head up.

and the central fissure of Rolando. The destruction was about 14 per cent (possibly more) of the total mass of the cerebrum,[2c] or one third of the mass of the frontal lobes. The amount of tissue removed at the time of operation was of course much less than this, as the direct destruction of both poles had been great at the time of the original injury, ten years earlier.

After completion of the operative procedures, the line of removal at the base was at about the level of the lesser wing of the sphenoid bone on each side, as shown in figure 4. In figure 3 the lines of removal in the left hemisphere are shown laterally by *AA* and medially by *BB*. The same sketch would serve approximately for the removal on the right. Both figure 3 and figure 4 were prepared from sketches made by the surgeon during the operative procedures and may therefore be considered fairly accurate, except that the actual removal was probably greater than is shown in figure 3, which is based on measurements taken from the frontal pole to the line of section, while figure 4 shows the relation of the line of section to the lesser wings of the sphenoid bones as it was actually observed.

The material was removed partly in a block (37.5 Gm.) and partly by suction. Of the excised block, at least half was estimated on pathologic study to be scar tissue. This specimen was excised according to the placed thread ties seen in figure 2. Further removal by means of suction was necessary in order to leave only tissue the circulation of which seemed to be satisfactory. The material removed by suction could not be reclaimed and weighed; it was almost altogether cerebral tissue, however, and its total volume may have been considerably greater than the amount of the specimen removed as a block.

Postoperative encephalograms showed clearly that there was little or no atrophy of the brain except in the frontal region (figs. 6 and 7), and the rest of the brain appeared to be grossly normal. Further, these encephalograms provided a valuable confirmation of the estimated extent of removal.

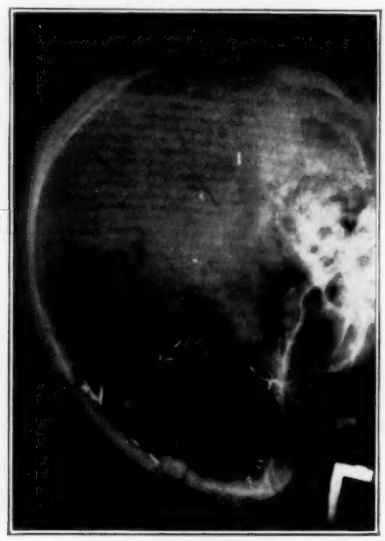


Fig. 7.—Pneumoencephalogram taken in the brow-up position, one month after operation.

There is an important difference between such a removal of an atrophic area and removal of a cerebral tumor. With atrophy, the brain tends to move toward the defect; with an expanding lesion, on the contrary, normal structures may be pushed away as much as 2 to 5 cm., and the apparent surgical removal of the greater part of a lobe may actually be the removal of little more than tumor tissue, leaving the displaced structures to return to their original positions. Thus, in general, excision of an atrophic area may result in a greater removal of normal structures, while excision of tumor may result in less removal than is apparent at the time of operation.

Another point of difference is the vascular change that may result from pressure from an expanding lesion, and the possibility of cellular destruction at a distance from the actual surgical excision. With removal of portions of the frontal lobes, preservation of the anterior cerebral arteries is extremely important

if one would make a judgment as to the degree of functional damage.[4] The two arteries often lie close together, and even with a unilateral approach it must often happen that one or both of these arteries is thrombosed or ligated. In this event pathologic changes and necrosis might be added to the surgical removal.

Even in the present case it must be admitted that, owing to disturbed circulation, the function of some of the anterior gyri may have been affected, although special

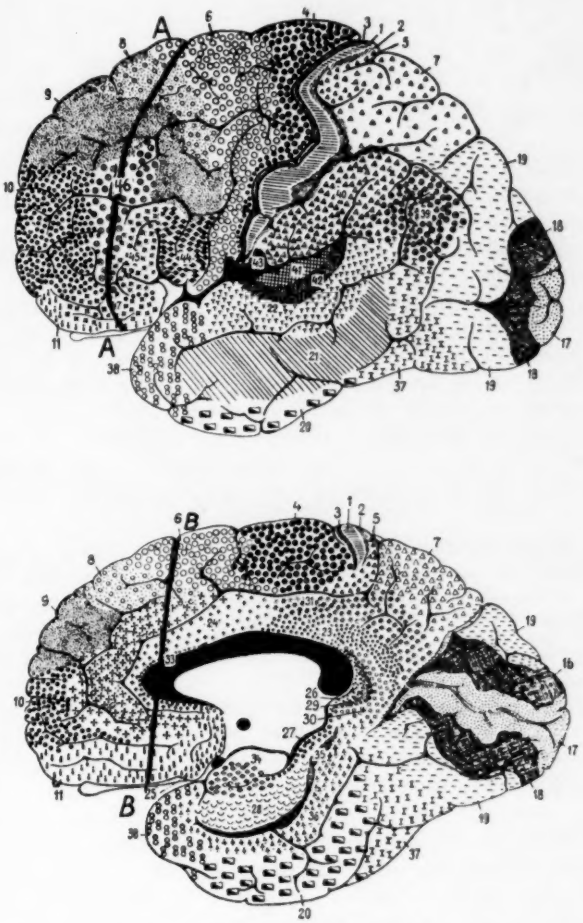


Fig. 8.—Diagrams showing the extent of removal of the cytoarchitectonic fields as mapped by Brodmann. *AA* indicates the estimated line of section on the lateral convexity of the brain of both sides (probably too far forward), and *BB*, the line of section in the median longitudinal fissure.

4. Critchley, M.: The Anterior Cerebral Artery and Its Syndromes, Brain **53**:120-165, 1930. Poppen, J. L.: Ligation of the Left Anterior Cerebral Artery: Its Hazards and Means of Avoidance of Its Complications, Arch. Neurol. & Psychiat. **41**:495-503 (March) 1939.

effort was made to prevent the possibility. The estimated destruction should therefore be regarded as minimum, not maximum.

Translation of the removal into terms of cerebral architecture can be done only approximately. From figure 3 it is evident that practically all of area 9 of the Vogts [5] was removed on both sides. In terms of Brodmann's map (fig. 8), the removal appears to include on each side all of area 10, all of area 9 except the posterior portion laterally, all of area 11 except a small tongue medially in the supraoptic region and a large proportion of areas 8 and 32, as well as some of the smaller areas 46 and 47. The exact cytoarchitectonic extent cannot, of course, be determined without histologic examination of tissue bordering on the line of section. Since the removal was completed by suction, this was not possible, and the probable extent of the lesion is shown in figure 8.

ANATOMIC COMPARISON WITH THE CASE OF BRICKNER

It is of interest to compare this case with that of Mr. A., a patient operated on by Dandy and studied exhaustively by Brickner.[1] It will be seen that our patient, K. M., showed little behavioral and mental defect of the kind described by Brickner.

Two explanations of the difference present themselves: 1. In removing a large bilateral frontal encapsulated tumor in two stages, Dr. Dandy found it necessary to amputate the frontal poles. In doing so the anterior cerebral arteries may have been ligated, with increased cerebral destruction. It is possible, therefore, that the symptoms described by Brickner were due to cerebral destruction which was greater than it was thought to have been. Mr. A. suffered from lasting symptoms of aphasia, although the surgical removal was in front of the speech area. It seems, therefore, that the destruction of tissue, in the left hemisphere at least, was greater than was apparent at operation, and this may have been due to circulatory occlusion.

2. The second possible explanation is that pathologic tissue left behind may produce interference with cerebral function. We hope to show later that in the case of K. M. operative removal produced great improvement in behavior and mental capacity. This is inconceivable unless the pathologic processes, set up by an epileptogenic zone of abnormal tissue, are capable of interfering with activity of the rest of the brain.

In Brickner's case the patient's mental condition was variable. This might indicate the presence of a pathologic influence, which is also suggested by the history of postoperative convulsions. Electroencephalographic study might have given evidence of subclinical seizures, particularly during A.'s bad periods. The variability of symptoms, the persistent jargon aphasia and the epileptic seizures all seem to show that A.'s condition was not due solely to the static removal of cerebral tissue as it was described in the operative notes.

PSYCHOLOGIC DATA

The psychologic data are of two kinds: those obtained with standardized tests and those obtained from observation of the patient and the reports of relatives. The psychometric data are extensive, and cover the period of the first postoperative year, with the results of a comprehensive examination on the patient's return to the clinic fifteen months after operation. Since the patient has been regarded by his family as still convalescent, data concerning adaptation to the demands of adult life must wait until he has had an opportunity to earn his own living. The emphasis

5. Vogt, C., and Vogt, O.: Die vergleichend-architektonische und die vergleichend-reizphysiologische Felderung der Grosshirnrinde unter besonderer Berücksichtigung der menschlichen, Naturwissenschaften **14**:1190-1194, 1926.

of the present report is on the striking improvement following operation, both clinically and psychometrically, and on the lack of the traditional gross signs of a lesion of the frontal lobe.

Psychometric Examination.—Immediately before operation the patient was examined with the revised Stanford-Binet and the McGill revision of the army beta test. Two months after operation he was examined with the Stanford-Binet, the revised beta and the Arthur revision of the Pintner-Paterson test. The Stanford-Binet and beta examinations were repeated at four and a half months after operation; finally, fifteen months after operation, a complete examination was made with these and other tests. A summary of the results with the composite scales is presented in table 1.

The preoperative intelligence quotient was 83. During examination with form L of the Stanford-Binet test there occurred a transient epileptoid state, of which the patient seemed unaware. For the first half-hour of the examination, in the vocabulary test and the year X items, the patient's answers were slow and of poor

TABLE 1.—*Preoperative and Postoperative Scores on Stanford-Binet, Arthur and Revised Army Beta Tests*

Test		Date	Score	Comment
Stanford-Binet.....	Form L	April 6, 1938	12-6 (I. Q. 83)*	Scatter X to Av. Ad.†
	Form M	June 1, 1938	14-2 (I. Q. 94)	Scatter VII to SA III
	Form L	June 13, 1938	13-4 (I. Q. 89)	Scatter X to SA I
	Form M	Aug. 30, 1938	14-8 (I. Q. 98)	Scatter VIII to SA II
	Form L	July 21, 1939	14-2 (I. Q. 94)	Scatter X to SA III
McGill revision army beta.....		April 7, 1938	63*	
		June 4, 1938	71	
		Aug. 30, 1938	65	
		July 22, 1939	75	
Arthur performance scale.....		June 3, 1938	33.25	No preoperative test
		July 21, 1939	43.65	

* Preoperative scores; operation was performed on April 9, 1938. Postoperative scores only are given for the Arthur scale.
† Av. Ad. means average adult (Stanford-Binet).

quality; they were quicker and better for the year XI items. When the patient was tested next day with the year X items on which he had failed, the answers were qualitatively as well as quantitatively improved, and were now satisfactory; there was little change in the vocabulary test except for increased speed of response.

This episode was detected only in the later improvement in behavior, and the patient denied that there was any change in himself or that he had had any kind of an attack. He seemed completely unaware of the period of slowing and deterioration.

Postoperative scores were consistently higher than preoperative scores, and there was no evidence of disparity of language and speeded nonlanguage abilities. The patient's scores were in general near the probable mean scores for the general population. Apparently, there are no data which permit comparison of adult levels on the Arthur and revised Stanford scales, but norms from Weisenburg and McBride [6] and Weisenburg, Roe and McBride [7] allow comparison of levels on

6. Weisenburg, T., and McBride, K. E.: Aphasia: A Clinical and Psychological Study, New York, Commonwealth Fund, Division of Publications, 1935.

7. Weisenburg, T.; Roe, A., and McBride, K. E.: Adult Intelligence: A Psychological Study of Test Performances, New York, Commonwealth Fund, Division of Publications, 1936.

the old Stanford vocabulary and other language tests with those on a number of nonlanguage tests. Unpublished results of experiments with normal control groups extend the comparison to include the Kohs block design test and a group of three experimental tests for adult clinical use, with good reliability. These tests, as yet not published, are a block manipulation test (delta E) analogous to the Kohs block test, a nonlanguage, unspeeded picture anomaly test and a language test of adult comprehension. The patient's scores on this battery of language and nonlanguage tests are presented in table 2, together with norms from Weisenburg and McBride or from the experiments referred to.

The results of two Rorschach examinations of K. M. will be reported in detail by Dr. Molly Harrower Erickson. During the first month of convalescence there was evidence of a serious personality disturbance, which, however, had completely disappeared on second examination, fifteen months after operation.

TABLE 2.—*Scores Made by K. M. Fifteen Months After Operation on a Battery of Homogeneous Tests* *

Test	Score	Norm	Comment
Stanford vocabulary	20	27	First half, old form
Weisenburg, Roe and McBride oral analogies	23	21 (23)	
Kelley-Trabue completion beta	7.05	7.8	
Adult comprehension	12	14	Experimental: verbal comprehension of social situations
Kohs block design	93	77 (80)	
Delta E	17	15 (16)	Experimental: analogous to Kohs test
Picture anomaly	15	14	Experimental: unspeeded, nonlanguage test
Mare and foal	33	29 (25)	Time score
Seguin	15	15.5 (15)	Time score
Porteous maze	13.5	14 (15)	
Healy completion I	646	..	Median normal score 511.5
Knox cube	7.5	..	Median normal score 7.4

* Probable normal adult mean scores are given, with norms for the 20 to 29 year group added in parenthesis for some tests. Three tests still in the experimental stage are included, and for these and the Kohs test the norms as given may be too high.

Other Observations.—The course of recovery has already been recorded, together with the clinical note from the summary made at the time of the patient's discharge concerning his mental status at that time. Other notes on his condition follow.

For the psychometric examination of Aug. 30, 1938, the patient had traveled some distance from his home. By an oversight, no arrangements had been made for his evening meal, and after the examination had gone on for about half an hour the patient mentioned that he was hungry. In doing so his manner was neither aggressive nor overapologetic. It took some time to obtain food, and in the meantime K. M. went on with the examination with undiminished effort. At no time was there any suggestion of distractibility or lack of restraint. Shifts from one kind of task to another were made readily; between test items the patient conversed normally with the examiner, and no abnormality could be detected in his manner or conversation.

When he returned to the Montreal Neurological Institute for a check-up after a year's absence, he spontaneously greeted by name a member of the staff with whom he had not much contact on his former visit, and showed an apparently normal recollection of the later part of his convalescence of the year before. It was interesting to find that he has no distinct memory of his condition or of many

events in the preoperative period. He said that his family had since told him about his behavior during that period, but he did not actually remember it. As far as could be ascertained, memory for events occurring before the original injury was good. Speaking of this, he remarked: "Since the operation I have noticed things coming back to me that I hadn't thought of for years."

The patient's father and brother are delighted with the change in K. Memory in everyday matters has improved greatly. Formerly "if he took it into his head to do something, you might as well talk to a post . . . Now you can depend on him, and if you talk to him he'll listen." They feel that he has changed from an irresponsible charge to one who is "just like any other person . . . 100 per cent improved." It is possible, of course, that his improvement has led to over-enthusiasm on the part of the relatives; the patient has not yet tried to earn a living. Information as to the patient's initiative [8] and ability to adjust himself socially and economically will have to be obtained later.

There are thus two aspects of the postoperative psychologic condition. One is his present clinical status and the result of psychometric examination, reported in the present paper. The other is the question of his eventual rehabilitation, about which nothing can be said at present.

COMMENT

One scarcely need stress the significance of the postoperative improvement in this patient. Before operation an injury in the frontal region and the formation of scar tissue had resulted in serious behavioral abnormalities. Further destruction, surgically, instead of aggravating the symptoms made them disappear. Even with the possibility that the improvement is partly due to altered outlook and fewer attacks, there could be no clearer demonstration of the detrimental effect of the presence of pathologic lesions in the brain.

The improvement of personality is particularly striking, but there is also one of intellectual capacity, as shown by the higher test scores after operation and by the improvement of memory for everyday matters. The improvement is seen chiefly in the results of clinical examination and in the history, but it should be noted that the preoperative intelligence quotient of 83 excludes the result of examination during the periods of slowing and deterioration, and is based on the retest scores, which showed the patient at his best before operation. Otherwise, the contrast with the postoperative intelligence quotient would have been greater. The improvement in the Rorschach record during convalescence, however, is significant; it is unfortunate that no preoperative examination could have been made, for this would probably have revealed more of the nature of the postoperative improvement. It is clear, of course, that the improvement is to be ascribed to a decrease of epileptogenic activity, not to removal of cerebral tissue as such. It would be equally absurd to suppose that the "normal" intelligence quotient, in the neighborhood of 95, after operation means that the patient's intelligence has not been affected by the injury and subsequent operation; neither is there any positive indication that the personality is quite unchanged. The important fact is the absence of grossly patho-

8. Penfield, W., and Evans, J.: The Frontal Lobe in Man: A Clinical Study of Maximum Removals, Brain **58**:115-133, 1935.

logic defects and of "frontal lobe signs." Although a psychometric level such as the patient's Binet score does not show that there has been no intellectual loss, the results of the tests provide positive evidence that any deterioration is not of the usual kind.

Intellectual deterioration due to mental disease has certain characteristics [9] which may permit its detection even when the Binet level remains fairly high. The deteriorated patient's scores in unspeeded language tests, particularly his vocabulary score, seem to be affected much less than his speeded nonlanguage scores. In the Binet examination this effect appears as "scatter," with the vocabulary score usually the highest or one of the highest. This situation is so frequently found with grossly pathologic conditions of the brain, as well as with schizophrenia, that it may be regarded as typical of intellectual deterioration.

From table 2, however, it may be seen that K. M.'s speeded nonlanguage scores compare well with his language scores, and that his vocabulary score of 20 on the old Stanford-Binet list is relatively low. In view of this fact the degree of scatter in the Binet examination (X to SA III, with vocabulary at the XIV year level) scarcely indicates the existence of postoperative intellectual deterioration—especially in view of the assertion of Harris and Shakow [10] that scatter is better evaluated by a point scale technic than by the subscores of composite tests, such as the Binet. Actually, it seems more likely in this case that any undue scatter is a result of the preoperative period of mental incapacitation, from the ages of 16 to 26, and life in a limited rural environment.

There seems also to be little question of "loss of abstract behavior" (Goldstein [11]). No difficulty in categorizing was found in a sorting test. This, and good performance in the Kohs test (one of those used by Goldstein), solution of "ingenuity" problems of the Stanford-Binet test, repetition of six digits backward and success with "essential similarities" in the same test indicate a reasonable degree of capacity for abstract thought. In this case, as in those of unilateral removal of the left frontal lobe,[2c] there was a striking lack of the so-called frontal lobe signs.

Thus, the postoperative status of the patient, clinically as well as psychometrically, does not suggest either intellectual deterioration or the personality changes which many writers have ascribed to injury of the frontal lobe. We must emphasize again that we do not suppose this to mean that no mental changes have taken place as a result of the injury to the frontal lobes; the loss of so much cerebral tissue must have had its effect, but it seems clear that the effect is not great, except as it may appear in the patient's future effort (or lack of effort) to rehabilitate himself.

---

9. Babcock, H.: An Experiment in the Measurement of Mental Deterioration, Arch. Psychol., 1930, no. 117.

10. Harris, A. J., and Shakow, D.: Scatter on the Stanford-Binet in Schizophrenic, Normal and Delinquent Adults, J. Abnorm. & Social Psychol. **33**:100-111, 1938.

11. Goldstein, K.: The Significance of the Frontal Lobes for Mental Performances, J. Neurol. & Psychopath. **17**:27-40, 1936. Goldstein, K., and Katz, S. E.: The Psychopathology of Pick's Disease, Arch. Neurol. & Psychiat. **38**:473-490 (Sept.) 1937.

The difference between this result and those reported elsewhere makes the case an important one in the study of function of the frontal lobes. The anatomic data are unusually good, and the lack of gross degeneration throughout the remaining cerebral tissue presents an opportunity to study the effects of a bilateral lesion restricted to the anterior third of the frontal lobes of the human brain. Gibbs, Gibbs and Lennox [12] have briefly reported a similar case, in which there was improvement after bilateral removal from the frontal lobes, but the only detailed account of a case comparable with ours is the report of Brickner.[1] It has already been noted that in the case of A. the surgical removal appears to have been complicated by pathologic destruction. As the postoperative improvement in our patient (K. M.) shows, abnormal cerebral activity in a region of pathologic change is capable of interfering with the normal activity of the rest of the brain, and the similarity of A.'s postoperative to K. M.'s preoperative condition suggests strongly that Brickner's findings were due to the presence of pathologic activity in addition to the surgical removal. The advantage in the present case is the apparent absence of complicating pathologic factors.

In any operation on the brain there is the possibility of vascular change and necrosis extending beyond the immediate field of operation. With good recovery, the presence or extent of the changes cannot be known. In not every case of removal of a tumor, of course, does this complication appear, but the possibility of its occurrence as the result of preoperative displacement and pressure, or of operative procedures, is greater than in a case of removal of an atrophic area. Published case reports [13] and the extensive psychologic study by Rylander [14] have shown that the effect of unilateral removal of a tumor of the frontal lobe may vary from no detectable symptoms to profound dementia, with a variability of symptoms in kind and degree which would be difficult to understand if the lesions were in fact similar. The assumption that in some cases the surgical removal has been complicated by vascular change and necrosis in the rest of the brain makes the variability understandable. It also implies, since the degree of pathologic complication is unknown in the individual case, that when the surgical lesion is of known extent the case in which the mental symptoms are fewest is likely to be best suited to the study of localization of function. The case in which there is the least apparent effect of removal is presumably the one in which there is the least pathologic destruction in addition to the surgical removal.

Since the anatomic data in the present case are good, it seems established that bilateral removal in man of the anterior third of the frontal lobes need have no obvious psychologic effect. This means, apparently,

12. Gibbs, F. A.; Gibbs, E. L., and Lennox, W. G.: Cerebral Dysrhythmias of Epilepsy: Measures for Their Control, Arch. Neurol. & Psychiat. **39**:298-314 (Feb.) 1938.

13. German, W. J., and Fox, J. C.: Observations Following Unilateral Lobectomies, A. Research Nerv. & Ment. Dis., Proc. (1932) **13**:378-434, 1934. Ackerly, S.: Instinctive, Emotional and Mental Changes Following Prefrontal Lobe Extirpation, Am. J. Psychiat. **92**:717-728, 1935. Jefferson.[2b] Penfield and Evans.[8]

14. Rylander, G.: Personality Changes After Operations on the Frontal Lobes: A Clinical Study of Thirty-Two Cases, London, Humphrey Milford, 1939.

that the postoperative symptoms described elsewhere, in cases of similar unilateral or bilateral removal, are not deficiency symptoms, and that cases of gross deterioration after limited destruction are not suited to the study of functions of the frontal lobes.

This must apply also to cases of mental change following pathologic destruction, such as those reported by Goldstein,[11] unless the actual cellular loss is greater than that we have described or is in a more critical region; however, except for Broca's area, there is no reason to regard the posterior part of the frontal lobe as specially significant in higher functions. Thus, the changes described by Goldstein may have followed a cellular loss greater than that of K. M.; but to show that "loss of abstract behavior" is an uncomplicated loss of function of the frontal lobe involves (*a*) proving that the lesion is wholly within the frontal lobes and (*b*) estimating the amount of cellular loss. In this one would encounter the primary difficulty of fixing the limits and extent of a pathologic lesion; Nichols and Weigner [15] have shown, for example, that the atrophy in Pick's disease may extend beyond the frontal region. If the difference between Goldstein's case and the one presented here were only in the degree of destruction within the frontal lobes, complete removal of a third of the lobes should be enough to produce behavior resembling somewhat that in Goldstein's case. Knowledge, on the other hand, that pathologic lesions of the frontal lobe may have a more deteriorating effect than complete loss of the region concerned makes it probable, from the evidence available, that the mental changes described by Goldstein are the product of cerebral dysfunction. Although no case of Pick's disease seems to have been studied electroencephalographically, cerebral destruction of this kind may be accompanied by abnormal electrical activity.[16] Such considerations do not affect the value of Goldstein's study as a psychologic analysis of a particular kind of deterioration, but indicate that the deterioration is not necessarily a simple loss of function of the frontal lobes.

The mental changes described by Freeman and Watts [17] after prefrontal "lobotomy" likewise do not seem to be due solely to the surgical destruction, which was described as anterior to the lateral ventricle and was therefore less than in the case we have reported. Their surgical procedure seems such as to produce extensive scar formation and vascular change, which might account for the observed mental phenomena. At any rate, if simple loss of tissue anterior to the ventricles can produce changes of behavior, complete removal back to and including the tips of the ventricles should produce greater changes.

The evidence in the present case, therefore, is opposed to the view that bilateral removal of the frontal poles, uncomplicated by pathologic processes, has a special effect on human intelligence or personality. This is not to be interpreted as evidence opposed to the demonstrations

15. Nichols, I. C., and Weigner, W. C.: Pick's Disease—A Specific Type of Dementia, Brain **61**:237-249, 1938.

16. Jasper, H. H.: Electrical Signs of Cortical Activity, Psychol. Bull. **34**: 411-481, 1937.

17. Freeman, W., and Watts, J. W.: An Interpretation of the Functions of the Frontal Lobe Based upon Observations in Forty-Eight Cases of Prefrontal Lobotomy, Yale J. Biol. & Med. **11**:527-539, 1939.

by Jacobsen and others [18] that bilateral removal of frontal lobe tissue has a specific, restricted effect on anthropoid behavior. A problem of interpretation is presented, but the phylogenetic difference between ape and man, and the necessary differences in test methods, are enough to preclude any opposition. Few clinical or experimental tests suitable for adult examination are independent of the complex learning processes accompanying human development; even if the patient is presented with a problem or test situation for the first time, solution involves to a great extent methods or forms of response established during the developmental period, and as such is probably not comparable with the ape's solution of delayed response problems in a laboratory setup.

For the effect of lesions of the frontal lobe on human intelligence, it seems that one will have to look elsewhere than to clinical observation or ratings by intelligence tests such as are now available. This is the more interesting because of the views generally held as to the importance of the frontal lobes in higher functions. The frontal region is the one to which has most frequently been attributed the development of higher behavior in man. The data by no means indicate that moral and intellectual functions are unaffected in our patient, but they are sufficient to show conclusively that he has not the kind of mental change which has been cited elsewhere as evidence of such an effect. If the frontal lobes, particularly the anterior parts (the development of which in man has been frequently stressed), were of primary importance in normal human behavior, the destruction we have described might reasonably have been expected to produce a definite defect. Some observers have accounted for the apparent lack of effect of unilateral lesions by the suggestion that one frontal association area can take over the functions of both; since we have shown, however, that there need be no more obvious defects following a comparable bilateral removal, this explanation, or the view that a second frontal lobe is supernumerary for the higher mental functions, has no longer any value.

For the present it seems that with the phylogenetic development from ape to man the function of the frontal lobes in behavioral organization has changed. It may be that no laboratory study will be adequate to reveal whatever defects follow frontal injury in man because of insufficient control of environmental factors and the difficulty of obtaining a good premorbid rating of ability. It may be that only in such features as learning in social situations, in adaptation to drastic environmental change or in initiative and the ability to plan and organize one's affairs [8] may be found the impairment that we believe must exist after large lesions of the frontal lobes, but of which we have found no evidence in the present case. It is clear that an apparent lack of effect on one type of ability does not mean that others are unaffected, as Lashley has pointed

18. Jacobsen, C. F.; Elder, J. H., and Haslerud, G. M.: Studies of Cerebral Functions in Primates: I. The Functions of the Frontal Association Areas in Monkeys, Comparative Psychology Monographs, Baltimore, Johns Hopkins Press, 1936, vol. 13, no. 3. Jacobsen, C. F., and Nissen, H. W.: Studies of Cerebral Function in Primates: IV. The Effects of Frontal Lobe Lesions on the Delayed Alternation Habit in Monkeys, J. Comp. Psychol. **23**:101-112, 1937. Finan, J. L.: Effects of Frontal Lobe Lesions on Temporally Organized Behavior in Monkeys, J. Neurophysiol. **2**:208-226, 1939.

out,[19] and further study of the rehabilitation of the patient may give some clue to behavioral defect following bilateral injury to the frontal lobes.

SUMMARY

In the case we have reported a traumatic injury had destroyed somewhat less than one third of each frontal lobe and left a scarred zone in each hemisphere, giving rise to continuing abnormal electrical potentials and to recurring epileptic seizures. Surgical removal of scars and a zone of grossly normal cerebral tissue, in such a way as to insure a minimum of scar, resulted in comparative freedom from attacks (two seizures in the fifteen months following operation, as compared with weekly seizures before). Although after operation a third, and possibly more, of the total volume of each frontal lobe was lacking, there was a striking postoperative improvement in personality and intellectual capacity, with the same medication as before operation. After the initial postoperative period no clinical or psychometric evidence of deterioration was detected.

It is obvious that abnormal areas of brain may produce, in a positive sense, both decreased mental capacity and abnormalities of behavior, and that absence of these areas may allow other parts of the brain to recover their normal functions. It is concluded that removal of a third of both frontal lobes, uncomplicated by pathologic change in the rest of the brain, need have no grossly deteriorating effect. The significance of this finding for the study of function of the frontal lobes is discussed.

19. Lashley, K. S.: Factors Limiting Recovery After Central Nervous Lesions, J. Nerv. & Ment. Dis. **88**:733-755, 1938.

MENINGIOMA IN A CHILD

J. Jay Keegan, M.D., Omaha

The following report of a meningioma which weighed 262 Gm. and was removed from the left parietal region of a child 8 years of age is presented because of the unusual size of the tumor, its occurrence at so early an age and the surprising lack of paralytic symptoms. Meningiomas are rare in childhood. Cushing,[1] in his series of 313 cases, reported that the youngest patient with an intracranial meningioma was a child aged 8 years; only 6 meningiomas were found in preadolescent children. A meningioma weighing 262 Gm. within the head of an 8 year old child equals about one quarter of the normal weight of the brain at that age. It would seem impossible for such a tumor to be present or to be removed without gross paralytic signs, yet both before and after operation there was only slight contralateral paralysis and little speech defect.

REPORT OF CASE

A white boy aged 8 years, who was referred to the Nebraska Methodist Hospital by Dr. Richard H. Young, had experienced the onset of generalized convulsions at the age of 18 months. These followed a fall downstairs to a cement floor, with a subsequent dazed condition lasting several hours. The generalized convulsions recurred two or three times a year during the next three years. He was then free from attacks for two years, but at the age of 5 years he began to have attacks of petit mal in which he would stop, stand still and spit. For a few moments he did not seem aware of what occurred; then he would resume his acticity. During this year he began again to have generalized convulsions at long intervals. He was given phenobarbital, which relieved the petit mal but not the grand mal attacks. At the age of 7 years signs of localization were first noted: Contractions began in the right hand, spreading to become generalized. Some weakness and numbness in the right hand followed and caused a gradual shift in predominant use from the right hand to the left hand. No alteration in speech was noted, and there was no mental deficiency, although because of his convulsions he was removed from school and protected at home. Lately the convulsions had been occurring almost weekly, often more than one in a day. The remainder of the history did not seem significant.

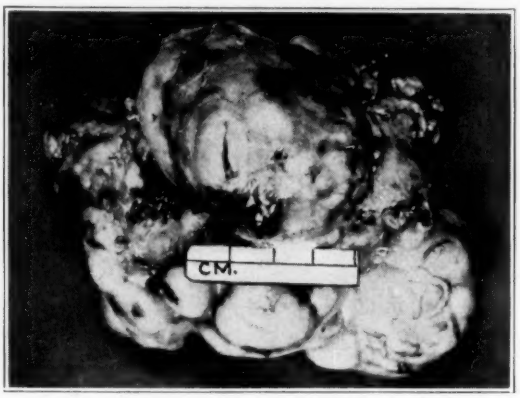
Examination.—In January 1938 there were palpable widening of the cranial sutures and a small elevation of very thin compressible bone in the left parietal region, near the arm center. There was slight motor weakness in the right arm, with associated generalized reduction of all forms of sensation. Astereognosis was prominent. Ophthalmoscopic examination showed papilledema of 3 D.; the spinal fluid pressure was 28 mm. of mercury; serologic tests gave negative results.

1. Cushing, H.: Meningiomas, Springfield, Ill., Charles C. Thomas, Publisher, 1938.

An encephalogram taken on January 22 showed marked thinning of the bone in the left parietal region, with abnormal underlying air shadows and failure of the ventricles to fill but with evident displacement of the midline structures 12 to 14 mm. to the right.

Diagnosis.—The impression from the preceding history and findings was that of a large tumor in the left parietal region.

Operation.—On January 25 a large left parietal bone flap was elevated without excessive bleeding. The exposed dura was tense and was torn at one place of adherence to the bone. A ventricular needle encountered firm resistance. Considerable fluid escaped from several small dural incisions, relieving the tension sufficiently to permit opening the dura with the base medially. At the site of the dural tear and bleeding there were dense adhesions to an underlying firm tumor, presenting at about the parietal eminence. Thinned, edematous and degenerated cortex surrounded this area from the medial border of the cerebral hemisphere to the temporal lobe and forward to the precentral region. A subarachnoid



Gross appearance of a meningioma weighing 262 Gm., taken from the left parietal region of an 8 year old child.

cystic area was opened in the anterior temporal angle. Deeper blunt dissection around the presenting firm parietal mass outlined a very large subcortical tumor which was firm, nodular and encapsulated. This extended so deeply that a possible origin from the petrous ridge in the floor of the skull was suspected. After considerable dissection and traction on the tumor the anterior border began to elevate, but deeper nodules could still be felt. The temporal border of the tumor was then freed, extending well into the temporal lobe. Here troublesome arterial bleeding occurred in a deep groove between two lobes of the tumor, but this was controlled by cotton packs and silver clips. A further attempt to free this vessel, thought to be the end of the lateral cerebral artery, caused bleeding again, and as vascular shock had developed further dissection was contraindicated. The dura was closed anteriorly and laterally but left open posteriorly. The bone flap was replaced and the scalp closed loosely.

Course.—The postoperative course after this first stage operation was fairly satisfactory, with recovery from shock in four or five hours, transient right hemiparesis lasting a few days and no marked aphasia. The wound remained clean and the bone flap somewhat elevated.

Second Operation.—This was performed on February 5. Dissection was extended about the lateral and posterior surfaces of the tumor, silver clips being applied to entering blood vessels. One large medial vein was ligated, the tumor being freed all around, and the growth was then gradually lifted out of its bed as deeper nodular projections appeared. There was no serious bleeding from the tumor bed. A thin, fluctuant membrane was seen in the deepest part of the large cavity, which was judged to be the wall of the lateral ventricle. The cavity was flushed and filled with physiologic solution of sodium chloride; the dura was closed, and the bone flap was replaced.

Course.—From this second stage operative procedure there was prompt recovery, with no additional hemiparesis. The papilledema gradually subsided, and the patient was dismissed from the hospital on February 22. There have been no recurrent seizures of petit mal or grand mal since the operation. The boy has returned to school and has normal mentality and speech. There is some residual sensory loss in the right hand, particularly to two point and object discrimination. Motor power is equal and good in all extremities; there are no abnormal reflexes.

Pathologic Report (by Charles P. Baker).—Grossly, the tumor measured 10 by 8 by 5 to 7 cm. It weighed 262 Gm. It was composed of many definite nodular growths, measuring up to 6 cm. in diameter (see accompanying illustration). These were closely held together and grossly gave an appearance similar to that of fibromyomas of the uterus. On section the masses were pearly white and firm. Microscopic sections revealed masses of long cells having a definite tendency to whorl formation; at the center of the individual whorl in some instances was a vessel or the remains of one. No calcification and no psammona bodies were observed. The pathologic diagnosis was meningioma.

SUMMARY

A 262 Gm. meningioma of the left parietal region of a child aged 8 years is described. Operation was followed by recovery, with relief of petit mal and grand mal, and the patient has normal mentality, speech and motor function.

Technical and Occasional Notes

A METHOD OF REPLACING NERVE FIBERS WITH FUSED GOLD

JOSHUA ROSETT, M.D.,† NEW YORK

The utility of the method in question consists in the greater clearness of the pattern of nerve fibers in microscopic preparations, brought about by disappearance of most of the background. It is limited to a rather low range of magnification—about 25 to 100 diameters—and to paraffin-embedded sections not much thicker than 10 microns. At higher magnifications defects in the picture, brought about by the fusion of some neurofibrils, become visible. Much thicker sections are apt to peel off the slide in the course of the procedure. The method is not applicable to the investigation of nerve cells, which in sections of such thickness become much shrunken. In considerably thinner sections, however, the shrinkage is slight and the nuclei and nucleoli appear clearly in a number of ganglion cells.

PROCEDURE

Sections of nerve tissue embedded in paraffin and mounted on slides with albumin, are stained by the method of Bielschowsky with silver and "toned" gold in the usual way. After drying, the slide is heated in the flame of a Bunsen burner. The colloidal gold fuses rapidly; the bluish or reddish color of the section disappears; the section becomes at first black, and then after the organic matter has become completely incinerated, yellow, like a gold mirror. The entire process takes less than a minute. After cooling, the slide is covered in the ordinary way.

Care should be taken to heat the thin end of the forceps, with which the slide is held in the flame, together with the slide itself, or the difference in temperature is apt to crack the glass. Any such accident is, of course, entirely avoided by mounting the preparations on mica cover slips.

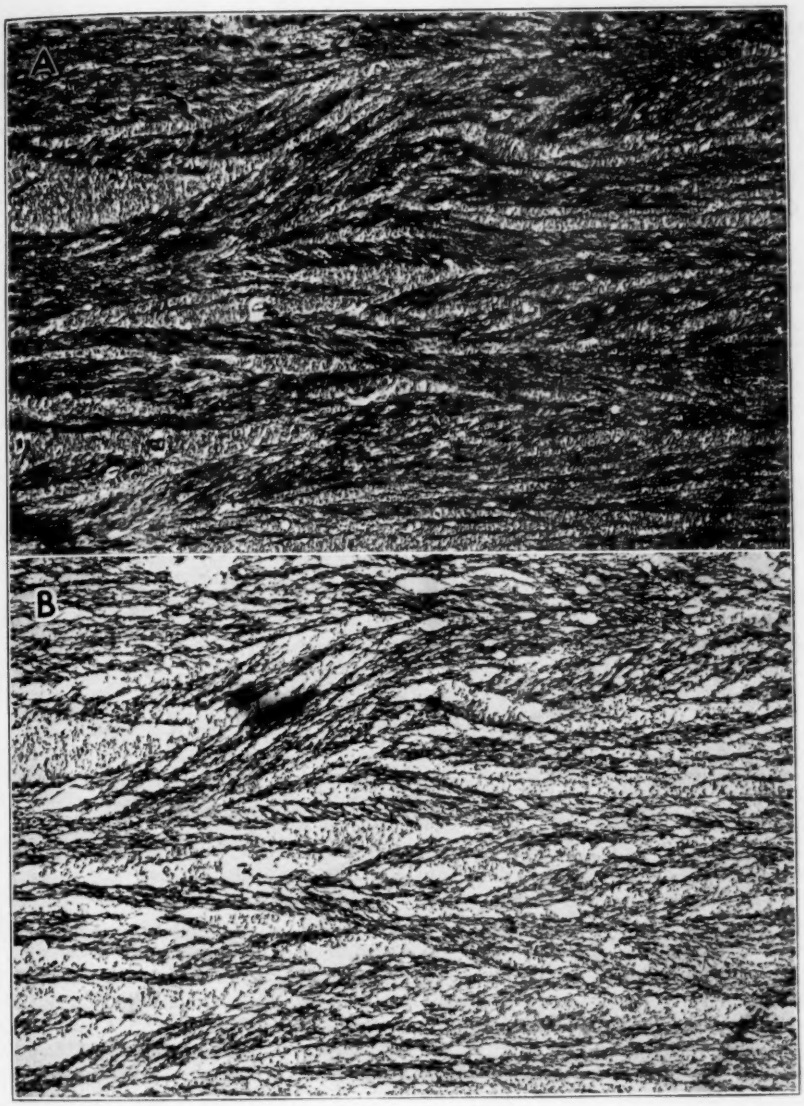
The accompanying photomicrographs illustrate the usefulness of the method.

---

† Dr. Rosett died April 1, 1940.

From the Department of Neuroanatomy, Columbia University College of Physicians and Surgeons.

The method described was evolved in the course of an extensive study of the neural connections of the basal ganglia as revealed by methods of silver impregnation, unfortunately left incomplete.—Editor.



Section from the human thalamus. *A*, Bielschowsky silver stain "toned" with gold; *B*, fused gold method. Magnification, about 50.

Society Transactions

PHILADELPHIA NEUROLOGICAL SOCIETY

TEMPLE FAY, M.D., *President, in the Chair*

Regular Meeting, Dec. 22, 1939

Cysticercus in the Fourth Ventricle: Report of a Case. DR. J. C. YASKIN and DR. ROBERT A. GROFF.

The reason for the report of this case is the unusual pathologic condition responsible for symptoms of tumor of the brain.

A white woman aged 30 was admitted to the Philadelphia General Hospital on Jan. 26, 1939, with the complaint of headache. She had been well until August 1938, when, during the seventh month of pregnancy, she noticed dimness of vision. One month later there developed nausea and vomiting. A month prior to admission to the hospital she experienced marked headache and double vision.

Neurologic examination revealed early papilledema on both sides, slight weakness of the superior rectus muscle of the right eye, slight asynergia on the left in the finger to nose test and a positive Romberg sign. Roentgenograms of the skull showed evidence of increased intracranial pressure, with thinning of the posterior clinoid processes and dorsum sellae.

After ventriculographic examination, a suboccipital craniectomy was performed. A tag of what appeared to be tumor tissue was observed arising from the floor of the fourth ventricle in the vicinity of the lower end of the aqueduct of Sylvius. This tissue was removed, and postoperative convalescence was uneventful. Histologic examination of the tissue revealed a cysticercus (Taenia solium). The larva was said to be dead.

DISCUSSION

DR. L. M. WEINBERGER: It is interesting that the cysticercus in the fourth ventricle produced vomiting on movements of the head, which I take to mean that the patient showed part of the syndrome first described by Bruns many years ago. He concluded that it is characteristic for a tumor of the fourth ventricle to produce intense vertigo, nausea and vomiting on movement of the head.

DR. E. SPIEGEL: The problem of Bruns's syndrome is interesting. In one group of cases the symptoms are explained by changes in the position of the tumor. However, one must bear in mind that a similar syndrome may appear without the presence of a tumor in the fourth ventricle. In these cases certain positions of the head may be associated with the appearance of nystagmus and/or vertigo. One must distinguish between two types of cases—one in which the labyrinth (probably the otoliths) is affected and one in which the rhombencephalon is the seat of disturbance.

Recently, my associates and I made experiments that may have some bearing on this. In cats in which the posterior part of the vermis was destroyed, rudimentary decerebrate rigidity and vertical nystagmus appeared. In these animals the nystagmus changed with the position of the head. These observations suggest that different positions of the head may have different effects on the vestibular nuclei if they are released from cerebellar inhibition. That may explain Bruns's syndrome in some cases.

Prolonged Stupor Produced by Subdural Hygroma: Relief by Trephine and Drainage. DR. MICHAEL SCOTT.

It is not generally known, except by neurologists, that a collection of clear subdural fluid, or so-called subdural hygroma, can produce symptoms similar to

those caused by any collection of subdural fluid or by a subdural clot. This is not a new subject, since Naffziger, Cohen, Dandy and Love have all written on it.

Three cases are reported. All the patients had an injury to the head, the result of an automobile accident, after which there was stupor lasting for from twenty-three to twenty-eight days before operation. At operation a unilateral or bilateral collection of clear subdural fluid was observed. After evacuation of this fluid the patients recovered and were discharged from the hospital.

Since an ounce (30 cc.) of clear fluid in the subdural space occupies as much volume as an ounce of blood or clot, it can be understood why a subdural hygroma produces symptoms identical with those of subdural hematoma or clot.

This type of lesion should be suspected in every case of injury to the head in which the usual tendency to recovery is not shown after proper measures for the relief of intracranial pressure and edema. The treatment is opening by trephine or burr, with drainage; if fluid is not found on one side or proper relief of symptoms is not obtained, the other side should be inspected.

DISCUSSION

DR. R. L. MASLAND: In a recent paper it was mentioned that a collection of fluid over the cortex does not produce any changes in an encephalogram, so that it is necessary to perform exploratory trephination.

DR. J. C. YASKIN: Is anything known about the pathogenesis of hygroma?

DR. L. M. WEINBERGER: Does Dr. Scott mean to imply that the prolonged periods of semistupor, or of stupor, are peculiar to subdural hygromas? Do they not occur as commonly with other types of accumulation of subdural fluid?

Elsberg and Cohen reported a case some years ago in which they aspirated more than 6,000 cc. of fluid from a hygroma in six weeks. They had to make repeated taps. The patient finally recovered.

DR. M. T. MOORE: I think Dr. Scott brought out an important point, namely, that in any case in which there has been an injury, irrespective of how severe it may have been, it is necessary to make a trephine opening on both sides because in some cases the evidence of accumulation of blood, or fluid other than blood, may be masked by the clinical condition of the patient.

DR. B. J. ALPERS: I wish to ask Dr. Scott whether it is necessary to operate in every case of this kind. I have seen a few cases in which there was evidence of fluid and recovery occurred without operation other than repeated lumbar puncture. Is it necessary to trephine in every case?

DR. TEMPLE FAY: Dr. Scott has selected 3 cases in which the period of unconsciousness was the outstanding feature. I have had a considerable number of such cases during the past fifteen years.

Dr. Weinberger asked whether stupor is a common phenomenon. I think that Dr. Scott's point is that consciousness returns promptly and other factors are recoverable with proper subdural drainage. The second point I should make concerns the operative technic. The neurosurgeon in the past has overlooked many of these conditions. I have called attention to the fact that an encephalogram may at first appear normal, except for slight flattening of the roof of the ventricles. A trephine opening measuring 2½ inches (6.3 cm.), however, reveals an increased amount of subdural fluid, which one drains; a flattened tube and wick covered by rubber dam are then inserted. The rubber dam drain is placed under the dura in the occipitotemporal area, because the patient will usually lie on the back and dependent drainage is required. The drain is brought out through a small notch in the trephine button, at such an angle that it can be easily withdrawn. It is my custom to retain this drain for from forty-eight to seventy-two hours; I have had no cases in which there has been infection. The relief of symptoms is remarkable, if drainage is continued beyond the twenty-four or forty-eight hour period.

I wish to emphasize that some patients can be relieved by opening the arachnoid cisterns at the base; one can drain this subdural fluid back through the posterior

fossa and spinal canal. I have seen this happen spontaneously during encephalographic examination. When one is in doubt a trephine opening should be made, for if fluid is present there will be a rapid change for the better in the patient's condition.

DR. MICHAEL SCOTT: I had not intended to leave the impression that there might be any symptomatic differentiation between a clot or a hygroma. One cannot tell which one is dealing with until operation. Little is known regarding the actual mechanism for the production of subdural hygroma.

Changes in Permeability in the Brain Induced by Metrazol and Insulin Convulsions. DR. E. A. SPIEGEL and DR. M. SPIEGEL-ADOLF.

The polarizability, and thus indirectly the permeability, of the cell surfaces was determined from five to ten minutes post mortem by measuring the conductivity at high and low frequencies on the exposed cerebral hemispheres at a temperature of 37 C. and calculating the polarization index. The normal values for the polarization index of the cerebral hemispheres varied between 11.9 and 17.8 per cent (mean 13.75 per cent $\pm$ 0.37). The brains of the animals subjected to metrazol convulsions showed values ranging between 9.4 and 12.9 per cent (mean 11.44 per cent $\pm$ 0.22). The influence of insulin convulsions was still more marked, the Δ values after these convulsions ranging from 8.4 to 12.3 per cent, with a mean of 10.84 per cent $\pm$ 0.24. The difference between the normal index and the index for the metrazol series was 2.31 per cent, with a probable error of $\pm$ 0.43; that between the normal index and the index for the insulin series was 2.91, with a probable error of $\pm$ 0.44. Thus metrazol and insulin convulsions, the latter somewhat more than the former, distinctly lower the polarizability of the cerebral hemispheres. This finding indicates that these convulsions increase the permeability of the cellular surface films.

DISCUSSION

DR. GEORGE GAMMON: Did the authors have an opportunity to follow the changes in this ratio during the course of insulin or metrazol administration?

DR. THOMAS K. RATHMELL, Norristown, Pa.: In patients under metrazol therapy I have observed the development of a meningitic type of colloidal gold curve in the cerebrospinal fluid—reduction levels ranging from 1 to 3. Perhaps the increase in cell permeability which Dr. Spiegel has demonstrated in animals treated with metrazol will serve to explain this phenomenon, the increased concentration of the metabolic products in the fluid due to increased cell permeability being the factor which reduces the gold solution.

DR. MANUEL PEARSON: Anything helping to reveal the mechanism of recovery following shock treatment of the psychoses will no doubt be of great value. At the Philadelphia General Hospital, anoxemia was produced in a series of patients by inhalation of nitrogen. Twenty patients were treated, but favorable responses were observed in only 2. Fifteen of the patients were subsequently treated with insulin and metrazol, with complete recovery of 9. In other words, although anoxemia may be of some benefit, it does not explain the whole mechanism of recovery.

DR. E. SPIEGEL: As to the relation between the nonelectrolyte-electrolyte ratio and the colloidal gold curve, Dr. Spiegel-Adolf found in all cases in which the colloidal gold reaction was positive an increase in this ratio, but an increase in the ratio is not necessarily associated with an abnormal colloidal gold curve.

With regard to anoxemia, I should hesitate to ascribe such a complicated mechanism as the therapeutic effect of these convulsions to one factor only. Anoxemia seems, however, to be one of the factors involved in metrazol as well as in insulin convulsions.

Myasthenia Gravis Associated with Pregnancy. Dr. Michael G. Wohl and Dr. Henry Wycis.

To date, there is little determinate information with regard to myasthenia gravis and pregnancy. Endocrine factors in the as yet unknown cause of the disease cannot be ignored when one observes the striking remissions during pregnancy and the relapses occurring soon after parturition. Three cases of myasthenia gravis associated with pregnancy have been studied at the Temple University Hospital.

REPORT OF CASES

Case 1.—M. G., aged 29, had become ill in 1929 with ptosis, strabismus and diplopia. She had been well maintained with ephedrine sulfate. During the entire period of her first pregnancy, in 1935, she had almost complete relief from symptoms. However, twenty days post partum, symptoms reappeared. Ephedrine and aminoacetic acid brought about temporary improvement. The addition of prostigmine bromide (15 mg. tablets, 6 to 8 a day) was sufficient to free her from symptoms and enable her to carry on ordinary household duties. In the second month of her second pregnancy, in 1937, she commenced to experience amelioration of the symptoms to an extent allowing reduction of prostigmine to 2 tablets a day. In the fourth month of pregnancy she felt more vigorous than she had for some time, despite the fact that she was taking prostigmine only occasionally. Use of ephedrine and aminoacetic acid was discontinued. Because of the marked improvement during pregnancy, it was thought that some endocrine factor might be responsible for the change. The pituitary gland appeared to be the most likely factor concerned. A lyophile serum was prepared from her blood obtained during the eighth month of pregnancy. The patient was delivered of a full term infant. Five days post partum she complained of weakness in the left arm and hand. Ten days after delivery there developed extreme weakness and dysarthria. Administration of prostigmine bromide, from 5 to 6 tablets a day by mouth, and ephedrine sulfate, ⅓ grain (0.024 Gm.) three times daily, controlled the symptoms. Two months after delivery the symptoms became worse, despite the aforementioned medication. Lyophile serum, 20 cc. daily, was administered for seven days. Soon after the second injection the fatigue was less pronounced, and after the fourth injection the patient commenced to feel so vigorous that prostigmine bromide was reduced to 1 tablet and ephedrine sulfate to 1 capsule a day. On the last day of the serum treatment she felt "normal," and omitted all medication. On the following day menstruation appeared. She experienced no weakness, as she had been accustomed to on previous occasions. Five days later the symptoms returned. Because the supply of serum was exhausted, the patient had to resort to 5 to 6 tablets of prostigmine bromide and 2 or 3 capsules of ephedrine sulfate daily. She is at present maintained satisfactorily on this dose, with relapse of symptoms shortly before menstruation.

Case 2.—C. M., aged 26, was referred to the endocrine clinic because of excessive gain in weight and extreme weakness. After the birth of her second child she noticed marked generalized fatigue, nervousness and dysphagia. She gained weight because she ate whenever she felt tired and nervous. The generalized weakness and dysphagia became more pronounced four to five days prior to menstruation. The patient had mild ptosis of the eyelids; otherwise the findings were normal. Intramuscular injection of 1 cc. of a 1:1,000 solution of prostigmine methylsulfate brought about marked improvement in the symptoms within ten minutes. The oral use of prostigmine with aminoacetic acid maintains her free from symptoms.

Case 3.—M. M., aged 37, lost weight and became weak after the birth of her third child. Because of these symptoms and a nodule in the isthmus of the thyroid gland, together with a basal metabolic rate of + 18 per cent, hyperthyroidism was thought to condition the symptoms. The administration of compound solution of iodine had no effect on the symptoms and caused no decrease in the basal metabolic

rate. Ptosis, dysphagia and dysarthria were noted. It is interesting that the latter symptoms were considerably worse a few days before menstruation. Prostigmine administered orally, with aminoacetic acid and ephedrine, gave marked improvement. The patient became pregnant in July 1938. During the first three months she was decidedly worse, despite the usual amounts of prostigmine, aminoacetic acid and ephedrine that had maintained her strength prior to the pregnancy. She was then given, at approximately five day intervals, twenty intramuscular injections of lyophilized serum obtained from the blood of women in the seventh to the eighth month of pregnancy. Her symptoms improved to such an extent that she reduced the prostigmine to half the usual amount. Ephedrine and aminoacetic acid were omitted. During the latter part of pregnancy she felt well, and resorted only to an occasional dose of prostigmine. The patient had a rapid, easy delivery and received no prostigmine afterward. On the fourth day after delivery she had a relapse, with pronounced weakness, dyspnea and cyanosis. The weakness was so marked that she was unable to keep her chin up owing to loss of tone in the masseter muscles. Administration of prostigmine intramuscularly and oxygen intranasally brought a dramatic response. The patient is at present satisfactorily maintained with prostigmine, aminoacetic acid and ephedrine.

Comment.—The defect in the production of acetylcholine is not the only pathophysiologic factor in myasthenia gravis. Likewise, an antiesterase action is not necessarily involved in the relief of symptoms following prostigmine. This is evident from the experimental work of Minot, Dodd and Riven and McGeorge. The 3 cases here reported emphasize the importance of the endocrine factors; 2 patients showed remission during pregnancy and responded favorably to the administration of lyophil serum obtained from pregnant women. All of them experienced aggravation of symptoms with each menstrual period.

The frequency with which symptoms of myasthenia gravis fluctuate during pregnancy and become aggravated with the menstrual cycle, and the improvement following the administration of serum from pregnant women in 2 of our cases lend support to the view that some endocrine factor may be implicated in the transmission of nerve impulses across the myoneural junction.

DISCUSSION

DR. A. SILVERSTEIN: The patient in the first case came under my observation at Temple University Hospital about five years ago. She then presented the clinical picture of well developed myasthenia gravis, with marked bulbar symptoms. Shortly after her discharge from the hospital she became pregnant. During this pregnancy her condition had improved to such an extent that her attending physician asked me to review the case, because it was believed that the diagnosis of myasthenia gravis was an error and that in all probability the condition was hysteria. Examination disclosed remarkable improvement in the myasthenic syndrome, but the symptoms of the disease were evident on careful examination.

About two months after being delivered of a dead baby, the patient was referred to me again by her physician, Dr. Helen Hays-Ryan. At this time she again showed the typical picture of myasthenia gravis. The bulbar symptoms appeared to be even more pronounced than before her pregnancy. From March 1936 to October 1937 the patient's condition was adequately controlled by injections of prostigmine methysulfate, in 1:2,000 solution, and tablets of prostigmine bromide. An interesting feature in the clinical picture during this period was the fluctuation of the symptoms in relation to the menstrual cycle.

With the onset of the patient's second pregnancy there again was noted prompt improvement in the myasthenic syndrome. In the second month medication was reduced from 8 to 2 tablets of prostigmine a day, and beginning with the third month of gestation improvement was so marked that the patient insisted she did not need any medication. However, she took 1 or 2 tablets up to the fourth month of pregnancy; she received little medication thereafter until the birth of a normal living child.

On noting the prompt remission during both pregnancies I became interested in this striking phenomenon, which suggested that the blood serum in pregnancy may contain substances which can modify the symptoms of myasthenia gravis. With this in mind, the advisability was discussed of preparing a concentrated form of the patient's blood serum, such as lyophile serum, in order to observe its effects on the return of the myasthenic syndrome. Unfortunately, I lost contact with the patient after her fourth month of pregnancy and do not know whether a concentrated serum was tried. The patient is now taking tablets of prostigmine.

DR. MICHAEL G. WOHL: Credit is due Dr. Wycis for his review of the current literature and presentation of our material. He has stressed two points: 1. Myasthenia gravis is probably more common than one is led to believe. We have seen, in a comparatively short time, 4 patients at the endocrine clinic of the Temple University Hospital. In 1934 Boothby reported 47 cases observed in the Mayo Clinic in a period of twenty-six months. The last patient whose case is reported here was referred to me for an opinion as to whether she should have surgical intervention or irradiation over the thyroid. Ptosis of the eyelids and the diplopia of which the patient complained led me to believe that the condition was myasthenia gravis rather than thyrotoxicosis; this was further proved by the course of the illness.

The second case was interesting to me because the patient was referred to the endocrine clinic with extreme obesity and various symptoms suggestive of a neurosis or some functional disturbance. She gained weight because she ate often and consumed extra food whenever she felt tired. The fact that she had ptosis of the eyelids and blurred vision whenever she tired was suggestive of myasthenia gravis. The prompt improvement with parenteral injection of prostigmine strengthened our clinical impression. A clearcut case is easy to diagnose. It is the progressive, slowly developing condition in an early stage that presents difficulties. The crux of the situation is to know when one is justified in attributing the symptoms to a functional disturbance and when to myasthenia gravis.

2. The disturbance in acetylcholine cannot explain the whole picture, because, as is well known if one gives a patient with myasthenia gravis acetylcholine, there is little or no improvement in the symptoms. Thyroid makes myasthenia gravis worse, and some cases have been reported in which the patients improved with the administration of anterior pituitary and insulin. Symptomatic fluctuation was shown by 2 of our patients during pregnancy; furthermore, improvement followed the use of lyophil serum of pregnant women. These observations make one believe that, although there may be some disturbance at the myoneural junction, other factors, probably related to the endocrine system, are implicated in the pathophysiology of the disease.

DR. G. D. GAMMON: Now that the question of acetylcholine is raised, it is well to recall that in order to obtain an effect on muscle, arterial injection is necessary. According to Lanari, injection of doses too small to cause contraction of normal muscles produces contraction of muscle in cases of myasthenia gravis. This suggests, but does not prove, that insufficient acetylcholine is liberated in the muscles in this condition.

DR. MANUEL PEARSON: During the past week Dr. A. E. Bennett, of the University of Nebraska, demonstrated in 2 patients at the Philadelphia General Hospital the effect of intramuscular injection of an alcoholic extract of curare, with the idea of reproducing a picture of myasthenia. The patients' reactions were interesting. They first had ocular symptoms, with bilateral ptosis and difficulty with extraocular movements, and later generalized muscular weakness. When 25 cc. of the extract was given and followed immediately by a dose of metrazol, the patient had a convulsive seizure of much less than the usual severity, so that it was not necessary even to place a tongue blade between the jaws. The duration of the convulsion was the same as usual, but there was less

agitation afterward. By using this procedure, Dr. Bennett claims to avoid the vertebral fractures and other complications of metrazol therapy. This drug reaction may throw light on the cause of myasthenia gravis.

DR. HENRY WYCIS: With regard to the esterase content of the blood: The data obtained are difficult to evaluate, since there is no satisfactory method for estimating esterase in the tissues.

NEW YORK NEUROLOGICAL SOCIETY

E. D. FRIEDMAN, M.D., *President, in the Chair*

Regular Meeting, Feb. 6, 1940

Comparative Pathophysiologic Alterations Produced by Increased Intraventricular Pressure. DR. E. JEFFERSON BROWDER, Brooklyn.

During the past four decades it has been generally accepted that the essential and clinically important effects of rapid increase in intracranial tension are the production of stupor, slowing of the pulse, rise in blood pressure and slow deep respirations, which if continued result in coma, racing pulse, falling blood pressure, rapid respirations, cyanosis and death. Furthermore, it has been taught that an estimation of these effects enables one to reckon the degree of intracranial tension and therefore conclusions arrived at from such an estimation may be used as a therapeutic guide. The unreliability of this hypothesis in the management of patients with cerebral trauma, in particular, led to a systematic investigation of the relation of the blood pressure, respiratory rate, pulse rate and cerebrospinal fluid pressure in a series of patients so injured. It was concluded from the study that the "classic pattern of signs" consisting of steady rise above normal levels of the blood pressure, slowing of the pulse, decrease in respiratory rate and stupor, which has been said to denote increasing intracranial tension, is rarely encountered after traumatic insults to the brain.

In a second study an attempt was made to evaluate the constitutional alterations produced by increasing the intracranial pressure alone, a group of patients with large cranial defects being used as subjects. The experimental setup was such that the intracranial tension, as measured in the lumbar thecal sac, could be changed within wide limits by applying pressure over the scalp covering the cranial defect. It was concluded from this study that no clinically significant alterations in blood pressure, pulse rate, respiratory rate and psychologic state were produced by raising the intracranial tension until the cerebrospinal fluid pressure, as measured in the lumbar thecal sac, reached or exceeded the level of the diastolic blood pressure.

This information, derived from the clinical and experimental investigations on intracranial tension, appeared to place this factor in a secondary role, at least with reference to its utility in accounting for the altered vital signs associated with severe trauma of the brain.

The question then arose whether pressure exerted from within the ventricular system might not prove adequate to alter the blood pressure, pulse rate, respiratory rate and mental state at a magnitude considerably less than that found necessary to effect such changes when applied to the external surface of the brain. Two series of experiments were carried out in this inquiry. The first consisted of eight experiments, 7 patients being used as subjects, each of whom had well healed parietally placed burr openings in the skull, previously made for diagnostic purposes. Each patient was ambulatory when submitted to the procedure necessary for the study. The method utilized was such that the intraventricular pressure could be elevated by the injection of physiologic solution of sodium chloride directly into the lateral

cerebral ventricle. The blood pressure, pulse rate, respiratory rate, pressure of the cerebrospinal fluid in the lumbar subarachnoid space, psychic state and alteration in vegetative functions were recorded at frequent intervals. The data derived from these experiments were similar to the recorded observations regarding vital signs in the experiments in which the pressure agent was applied to the external surface of the brain, in that no appreciable changes in the blood pressure, pulse rate and respiratory rate were observed until the intraventricular pressure reached or exceeded the level of the diastolic blood pressure. In 2 instances the blood pressure became elevated after the intraventricular pressure produced by the injection had receded, and in 1 of these cases the blood pressure remained considerably elevated for nine hours. The results of the experiments were not entirely satisfactory, since a desired level of increased intraventricular pressure could not be maintained without the continuous injection of solution of sodium chloride, a procedure seemingly not without danger to the subject.

Further investigations were therefore carried out, with the dog as the experimental animal. The experimental setup was similar to that employed in man, except for the recording of the pressure in the spinal subarachnoid space by means of a needle placed in the cistern rather than in the lumbar thecal sac and the making of a continuous instead of a minute interval kymograph record of the intraventricular pressure, cisternal pressure, respiratory rate, blood pressure and pulse rate.

The information gained from an analysis of these twenty-one experiments lends support to the conclusions arrived at from the data recorded in the human experiments, namely, that rapidly increasing intraventricular pressure does not produce significant alterations in the pulse rate, blood pressure and respiratory rate until the intraventricular pressure reaches a level equal to or slightly in excess of the diastolic blood pressure. In addition, it was observed that an intraventricular pressure of a magnitude much less than the level of the diastolic blood pressure (60 mm. of mercury) if maintained for several hours produced significant alterations in the blood pressure, pulse rate and respiratory rate.

These findings suggest that the length of time the pressure is sustained takes a place of equal importance with the rapidity of application of the intraventricular pressure, as well as its degree. This time element has received too little direct attention in consideration of the effects of an agent producing increased intracranial tension.

DISCUSSION

DR. SAMUEL BROCK: In a previous valuable study, Dr. Browder and Dr. Meyers emphasized that in cases of acute injury to the brain the "classic signs" of increased intracranial pressure are of little help, singly or in combination, in determining the level of intracranial tension. These signs are the steady rise of blood pressure above normal levels, the slowing of pulse and respiratory rates and the presence of stupor or vomiting, followed later by falling of blood pressure, development of fast pulse and respiratory rates and cyanosis. Together with others, these authors showed that no prognostic information could be derived from single or repeated determinations of cerebrospinal fluid pressure in cases of acute injury to the brain.

In pursuing these studies further, Browder finds that the intracranial tension must reach or exceed the level of the diastolic blood pressure before significant alterations occur in blood pressure, pulse and respiratory rates and psychic state. He has shown that it does not matter whether the pressure is raised by extracerebral or intraventricular factors if the time interval is short. However, the maintenance of intraventricular pressure at a raised but still subdiastolic level for several hours did produce significant alterations in blood pressure and pulse and respiratory rates.

These important studies throw further light on the function of the vital centers in the medulla governing blood pressure, pulse rate and respiration. Obviously, there is close interlocking of these vital functions, so that once peripheral resistance is raised to diastolic or supradiastolic, or even to certain infradiastolic, levels and

long maintained in as sensitive a vascular bed as that of the brain local impairment of circulation results. Then the cardiovascular and respiratory centers respond to their altered physicochemical environment in such a way as to prevent the oncoming anoxia.

All these studies show that one cannot depend on estimations of blood and cerebrospinal fluid pressure and on pulse and respiratory rates in treating patients with acute injuries to the brain—nor are these data of much prognostic value.

Urinary Incontinence of Cerebral Origin. Dr. Abraham M. Rabiner and Dr. Orman C. Perkins, Brooklyn.

The role that the cerebrum plays in vesical activity has attracted considerable attention. We are not at this time particularly concerned with controversies as to the precise localization of such cerebral centers.

The clinician long has been aware of the fact that sphincteric symptoms should immediately direct his attention to a clinical syndrome which has affected the spinal cord. It has therefore at times been confusing to hear reference made to suprasegmental regulation of reflex vesical activity. It seemed to us that clarification of the type of sphincteric disorder which could be ascribed to cerebral control was necessary.

Loss of control of the sphincters with resulting involuntary urination is not an uncommon observation in the practice of every physician. When it is the result of disease of the spinal cord the patient voids urine, realizes that this is taking place and yet cannot voluntarily halt the stream. He is alert and fully conscious, with no impairment of cerebral faculties. He has a disorder in the spinal reflex control of bladder function. This reflex may be voluntarily inhibited or aided. The extent of violation depends on the degree of consciousness. A person in deep coma cannot exert voluntary activity, and the will varies with levels of consciousness. In urinary incontinence associated with lesions of the spinal cord the patient is aware of the incontinence but cannot halt the urinary stream. In incontinence due to cerebral disease there is usually a picture of mental disturbance, varying in degree from indifference and apathy to somnolence and stupor. The hypothalamus undoubtedly plays a role in the involuntary urination occurring during episodes of sudden fright or panic. We believe that involvement of both cerebral hemispheres is essential for the occurrence of urinary incontinence when the function of the spinal cord is normal. This may be compared with the bilateral cerebral lesions of the pseudobulbar syndrome. It appears to us that in cases in which isolated cerebral lesions are alleged to be the cause of urinary incontinence there must be at least a momentary interruption of consciousness. To illustrate this, we present the following case from the service of Dr. Jefferson Browder.

M. A., a man aged 51, was employed as a motorman. In October 1933, his trolley car ran into a truck. He did not sustain any injuries. In the subsequent ten months there gradually developed weakness in the right upper and lower extremities. Later there was a change in personality, with impairment of memory and urinary incontinence. On Aug. 24, 1934, craniotomy was performed and a meningioma removed from the left frontal region. The incontinence of urine in this case was regarded as occurring when the man was fully conscious. Careful questioning, however, revealed that while performing his duties as a motorman, he would suddenly become aware that he was standing in a pool of urine. He did not know that he had voided, and did not even feel that his clothes had become wet. It is obvious, therefore, that the incontinence did not occur in a fully conscious state, but was part of a petit mal seizure.

Conclusions.—1. Urinary incontinence results from a single unilateral focal lesion only when the pathologic process affects the spinal center in the lumbosacral region of the cord.

2. Urinary incontinence can occur as a result of bilateral cerebral lesions. Here the mechanism may be considered identical with that observed in pseudo-

bulbar palsy, and consists in cutting off of the bilateral supranuclear connections that are available for all so-called vital functions.

3. Urinary incontinence is associated with single unilateral cerebral lesions only when there is impairment of consciousness.

DISCUSSION

DR. ISRAEL S. WECHSLER: The authors have made a few statements which will bear challenge. First, it seems to me that incontinence of urine of which the patient is unaware as a rule occurs in disease of the spinal cord, unless the lesion is so minute as not to impair the sensory pathways. Incontinence with normal mentality, therefore, and unawareness of wetting is nearly always significant of lesions of the cord. When a patient is unconscious or his consciousness is markedly impaired he does not have general sensation and so does not feel anything, whether it is the passage of urine or some other stimulus.

I think Dr. Rabiner and Dr. Perkins have omitted mention of a large center in the brain outside the paracentral lobule or other cortical and subcortical regions where a lesion may cause impairment of the urinary function. It is known clinically that in epidemic encephalitis retention of urine may be the first symptom. This was commonly observed in the early days of the epidemic. Distention of the bladder was sometimes extreme, but incontinence was infrequent. Retention may occur, however, with lesions of the upper or lower portion of the midbrain or with disease of the interbrain other than inflammation. To mention 1 instance: A young woman had retention of urine which was diagnosed as hysteria. She was catheterized several times; the retention receded for a few days and then recurred; again the diagnosis of hysteria was made. It was only when palsy of the sixth nerve appeared that the possibility of a lesion of the brain dawned on the examiner. It was on evaluation of the symptom of retention of urine, in addition to vertical nystagmus, that I ventured the diagnosis of intrapontile lesion extending into the midbrain. Autopsy revealed a tumor in this area. Here, then, is a region of the brain impairment of which will give rise to disturbance of urinary function.

It has also seemed to me that incontinence of urine in an epileptic attack is not merely a symptom of unconsciousness but a sign of some focal significance, just as the epileptic cry is not a symptom merely of expulsion of air through the larynx. The cry occurs only in certain persons; it has been demonstrated on the operating table by stimulation of certain parts of the cortex. Urinary incontinence in epilepsy may be a focal sign, and that is why it does not occur in all epileptic patients.

In conclusion, I may say that there are four kinds of urinary incontinence or impairment of urinary function: (1) that due to lesions of the spinal cord, in which there is apt to be local loss of sensation; (2) that due to general impairment or loss of consciousness, which the authors have so well described; (3) that due to focal lesions in the paracentral lobule, and (4) that which results from impairment of function by lesions in the upper portion of the midbrain, or possibly the lower regions of the interbrain.

DR. FRITZ CRAMER: I wish to add that involvement of the paracentral lobule, particularly by tumor, is apt to cause incontinence. This may happen even when the tumor is in the nondominant hemisphere and there is no destruction of the patient's critical faculties. I have in mind several such cases in which there was a focal tumor in the motor area and paracentral lobule which caused precipitate micturition with full consciousness and mental awareness. The neoplasms were mostly meningiomas, of the eroding vascular type, as well as infiltrating gliogenous tumors. This type of incontinence has not been observed frequently, but one should bear in mind that it does occur.

DR. ISRAEL STRAUSS: Did the authors say whether micturition is an involuntary or a voluntary act?

DR. ABRAHAM M. RABINER: It may be both.

DR. ISRAEL STRAUSS: Is it more often involuntary than voluntary?

DR. ABRAHAM M. RABINER: No.

DR. ISRAEL STRAUSS: I gained the impression from the paper that it was more often involuntary than voluntary. I also thought the authors stated that they would not discuss voluntary and involuntary function. I did not know that the act of micturition was entirely involuntary, or largely so. It seems to me it is completely under the control of the higher centers. I appreciate the fact that panic and emotional states also can cause involuntary micturition, but I know, too, that a panic state can cause retention of urine. Any person may find himself pressed to urinate, ready to do so, when a sudden situation of embarrassment arises and he cannot void a drop, full as his bladder may be. Hysteria also can cause complete retention of urine.

What the authors have stated regarding tumors of the brain has long been known; in fact, in a study of a great number of cases of tumors with mental symptoms, incontinence was found frequently but always in association with a change in the sensorium and never as a focal symptom; I believe that while the paracentral lobule may have a center, there are unquestionably centers below in the hypothalamus and probably, as Dr. Wechsler said, even lower. When one comes to study incontinence in the case of lesions of the cord, whether complete or otherwise, it is not sufficient merely to state that the patient is incontinent. It is important to employ exact cystometric methods, as has been done by Langsworthy and Simon. One will find a great variety of bladder conditions secondary to lesions of the cord; in some cases a hypertonic bladder is the cause of the incontinence, in some a paralytic bladder and in others actual hypertrophy of the sphincter. In certain cases one will find on cystometric examination that although the sensation of pain is present stimulation of the parasympathetic nerve mechanism produces an irritable bladder and involuntary urination. All these factors must be studied in deciding on the nature of incontinence associated with a lesion of the cord.

I believe that Dr. Rabiner and Dr. Perkins are correct in stating that in the case of cerebral pathologic conditions, particularly tumors, one is dependent on disturbance of the sensorium to account for the incontinence. Dr. Wechsler said inflammatory lesions, such as encephalitis, have been shown to cause this disturbance. However, I have never seen incontinence in the early stages of encephalitis and, in view of the pathologic changes in encephalitis, one must consider that in such cases one is dealing with irritation of the deeper centers of the brain concerned with sympathetic bladder function.

DR. E. D. FRIEDMAN: I wish to say a few words in defense of the thesis presented here. I may remind my associates who served with me in the wards of Mount Sinai Hospital that we had an opportunity to observe a man who showed signs suggestive of multiple sclerosis. He presented bilateral spasticity of the lower limbs, optic atrophy and vesical incontinence. It was proved later that he had a pituitary tumor, which grew upward through the corpus callosum and was situated between the paracentral lobules. One therefore must admit the possibility of incontinence of urine from a lesion involving both paracentral lobules.

DR. ABRAHAM M. RABINER: Dr. Wechsler said that during the epidemic of encephalitis patients had incontinence. I am not concerned with the pathologic picture, though it is evident that in encephalitis with multiple lesions the cord as well as the brain may be involved. I shall stress only that when the lesion is only in the brain difficulty in sphincteric control is due either to bilaterality of the lesion or to some disturbance in consciousness. Lesions of the pons affect bilateral structures. If a patient is fully conscious and has a unilateral cerebral lesion urinary incontinence does not occur.

The case presented is an illustration of the error made when it is stated that the patient loses control of the bladder and is conscious. I maintain that a patient who has urinary incontinence as the initial symptom of an epileptic attack has already lost consciousness when he passes the urine.

This applies also to Dr. Cramer's discussion. Patients with lesions of the paracentral lobule who are incontinent and appear to be fully conscious must be

regarded as subject to petit mal seizures. The attacks may be transitory. Urinary incontinence resulting from an isolated lesion of the brain occurs only when consciousness is clouded or lost; when the lesions are bilateral the mechanism is the same as that in pseudobulbar palsy.

I agree with Dr. Strauss that in panic states either urinary incontinence or retention may occur; in one it is a sudden propulsion of urine; in the other it is a state of tension preventing urination. Both are the result of panic. Cystometry deals only with a local tension state of the mucosa of the bladder in response to the volume of urine. This varies and gives rise to stimuli which travel up to the brain and produce incontinence only if there are bilateral cerebral lesions or a unilateral cerebral lesion with some degree of altered consciousness.

Surgical Procedure for Postencephalitic Tremor, with Notes on the Physiology of Premotor Fibers. DR. H. RUSSELL MEYERS (by invitation), Brooklyn.

That therapy directed toward relief of chronic sequelae of the encephalitides has been of a generally disappointing character is best attested to by the wide range of agents employed during the past twenty years. Reference to the reports of the Matheson Commission, in its publications of 1929, 1932 and 1939, indicates that under one circumstance or another almost every medicinal agent known to the pharmacopeia—dietary, drug and biologic—has been tried. With few exceptions, chief among which stand the belladonna derivatives, these have proved of small value. Similarly ineffectual has been the application of the various physical therapy technics—mechanical, thermal and radiant. Psychotherapy has been employed not only for the more obvious neurologic syndromes, such as the parkinsonian states, oculogyric crises and convulsive disorders, but also for the postencephalitic psychoses and problems of childhood behavior. The critical experience of most writers has been that these aberrations are singularly refractory to psychotherapy.

During recent years several surgical procedures have been devised to deal with the tics, tremors and rigidity encountered in the parkinsonian states. Among such operations, sympathetic ramisectomy and ganglionectomy enjoyed a wide vogue between 1923 and 1935. Dorsal and ventral rhizotomy was only less frequently employed during the same period. If one may judge from present day reports, these operations have largely been abandoned. Phrenicectomy has been usefully employed on occasion for diaphragmatic tics. More recently, the central nervous system has been attacked by Bucy and by Putnam. Bucy extirpated portions of the cortex of the premotor and motor areas in 2 patients. One of these had posttraumatic unilateral tremor of both resting and intention type. The second presented a more characteristic parkinsonian picture. Effectual relief from tremors was obtained by the procedure, although a degree of paresis and considerable dyspraxia in the affected limbs supervened. Putnam sectioned the extrapyramidal tracts in the spinal cord in 5 cases. Encountering disappointment, he then, in 2 cases of hemiparkinsonism, sectioned the pyramidal tracts at the upper cervical level. Gratifying improvement was obtained in both these cases. Of no less interest was the survival in the involved limbs of functions which traditionally have been imputed to the pyramidal tracts. Machansky used the Putnam operation in 17 cases. In this series, 4 patients died, 5 were somewhat improved and 3 recovered.

One year ago, a mulatto woman aged 26 was admitted to the neurosurgical service of the Kings County Hospital with a severe tremor on the left side when at rest. The tremor had followed by two months an influenza-like infection, and had been present for seven years. Her social, economic and home life had been so disrupted by the tremor that she sought amputation of the left arm. Neurologic examination gave essentially normal results except for the rhythmic tremors and parkinsonian facies. Encephalograms were normal. Electroencephalograms, taken from over the right premotor and prefrontal areas, revealed anomalous bursts of action potentials of high voltage and obvious dysrhythmia. Electromyograms of

the left limbs disclosed spindles of rapid frequency and high voltage coincident with phases of increased amplitude of the clinically observable tremors. Psychometric examinations, blood chemical analysis, urinalysis, serologic tests and readings of skin temperatures revealed nothing remarkable. On March 7, 1939 a right osteoplastic bone flap was reflected, with use of local anesthesia. After identification of the excitable motor cortex with bipolar electrodes, a section was made through the cortex and into the white matter to a depth of 3.5 cm. As far as could be determined grossly, this passed through the so-called strip area in such a manner as to sever from the sagittal line down to the operculum the U fiber coursing between areas 4 and 6. The tremors were unaltered by this procedure. In line with an idea suggested by Bucy's operation, the entire premotor area was next undercut at a depth of about 3 cm., the intention being to interrupt the pathways between area 6 and the subcortical nuclear structures. The tremors persisted unaltered. On the hypothesis that hyperkinesis is subtended by the neopallium in diseases of the basal ganglia, the right caudate nucleus was exposed through a prefrontal incision into the anterior horn of the lateral ventricle and the anterior two thirds of its head extirpated. The patient was observed closely for vegetative and somatic manifestations of the so-called premotor syndrome. These did not appear. Abolishment of the tremors has persisted until the time of this report, except for their transient presence during states of high emotional excitement, such as anger and orgasm. Dyspraxia and paresis have not been noted. The apathetic facies has apparently disappeared. As far as can be observed, no psychologic or physiologic disabilities obtain. The postoperative performance in the psychometric tests was substantially unaltered. The postoperative electroencephalograms and electromyograms assumed essentially normal characteristics.

On Nov. 29, 1939 a man aged 39 with typical bilateral parkinsonism was subjected to extirpation of the head of the right caudate nucleus. Immediate benefit was noted. The tremors of the left extremities were entirely absent for many minutes, and reappeared only when the tremors of the right extremities were in an active phase. At such times the amplitude of the tremors on the left was between 10 and 25 per cent of that formerly present. Furthermore, there was an estimated reduction of 25 per cent in the tremors of the right limbs. Since bilateral anatomic representation is recognized in the ansa lenticularis, it is probable that the reduced tremors now observed in the left limbs are subtended by ipsilateral neural motivators responsible in large part for the tremors in the right limbs. The rigidity of the left hand was obviously improved for the execution of eupractic functions, as compared with the preoperative performance. The simian posture, masked facies and "greasy" complexion were unaffected. It is planned to carry out a second operation, with extirpation of the left caudate nucleus.

A woman aged 26 with severe tremors and moderate rigidity of the right limbs, of seven years' duration, was subjected to extirpation of the entire head of the left caudate nucleus on Jan. 25, 1940. The tremors to date have remained completely in abeyance, but since hemiparesis supervened after operation (presumably due to an unusual degree of cerebral edema) and has only within the last three days begun to subside, it is somewhat premature to speculate on the outcome. Nevertheless, with return of voluntary functions of the lower extremity no tremors have been noted, a circumstance which is promising, as the tremors of paralysis agitans when interrupted by a cerebrovascular ictus in the capsule regularly reappear with return of control of the affected limbs.

Two physiologic observations worthy of note in connection with the surgical procedures described are recorded. First, it is evident that with preservation of the integrity of the premotor cortex discrete neural pathways are as unnecessary for the mediation of impulses involved in the execution of skilled acts and perceptual responses (incitograms) as they are for perceptual engrams and other higher psychologic processes. Second, the caudate nucleus can apparently be ablated without "releasing" any clinically observable anomalous neural patterns.

Speculation on the role of the caudate nucleus in postencephalitic tremor naturally arises. My present conviction is that the caudate nucleus does not initiate

the impulses which give rise to tremor, but rather is an indispensable part of the suprasegmental loop which mediates such impulses. Several reasons underlie this conviction. First, with intense emotional stimuli the tremors, though evanescent, reappear; second, and more significant, electrocorticographic action potentials taken directly from the premotor and prefrontal zones disclose slow sinus rhythms with a frequency of 4 per second coming in spindles that are synchronous with the exaggerated phases of clinical tremor, whereas action potentials led off from the caudate nucleus itself by means of an Adrian-Bronk needle show no such electrical phenomena.

It is evident that the findings raise many more questions than they can explain.

(A motion picture showed the patients and the essential features of the operation.)

DISCUSSION

DR. TRACY J. PUTNAM: This is a brilliant attack on an old and extremely troublesome problem. Every neurologist knows how distressing tremor may be to the patient. Four years ago surgical intervention was scarcely thought of as a possibility for patients suffering with paralysis agitans; now the question is not whether anything can be done for such patients, but which is the preferable procedure in each case. Dr. Meyers' method, as presented, seems to have certain advantages over the two slightly older procedures. The patient certainly has less immediate postoperative disturbance than with the other procedures, and probably in the long run less disability. Against this must be weighed the greater extent of the operation, and presumably its greater danger as compared with that in the simpler operations. An important point in regard to the cortical operations is that the tremor can be greatly modified by operations which do not involve area 4. In Bucy's original case he removed both area 4 and area 6. Dr. R. M. Klemme, of St. Louis, has operated in a large series of cases; I understand his technic consists in removal of the cortex anterior to the motor strip. He has not published his results, however, and one cannot be certain what the extent of removal or the end results have been. I have seen the results of treatment with chordotomy; I have also had some experience with the cortical operation and find that removal of area 6 will modify the tremors without much interference in function, although there is more immediate postoperative disability than occurred in the first 2 cases reported by Dr. Meyers.

There is bound to arise the question whether the cortical incision which Dr. Meyers makes and the operative procedure are not enough to injure the projection fibers from the cortex and so produce the same physiologic result as is obtained with the older operations. That this is not the case appears from the fact that in 1 of my cases infiltration with procaine of the portion of the cortex with which he works had no effect on the tremor. Moreover, if there has been subsequent interference with the pyramidal fibers there would have been more disability than was seen in the first 2 cases. I think, therefore, that this is an important contribution to the surgical treatment and to the physiology of paralysis agitans.

There are some theoretic points on which I find it hard to agree with Dr. Meyers. First, I believe as a result of my own studies that area 6 forms part of the stimulable motor cortex, and that the region which was undermined in Dr. Meyers' patient was that anterior to area 6, which lies chiefly on the surface of the precentral convolution, while area 4 lies practically hidden from view in the depths of the rolandic fissure. Second, I do not feel certain that these results can be taken as a substantiation of Lashley's views. I think that if Dr. Meyers' incision had been a little farther back, actually in the motor strip, or if it had been in the temporal region or on the inner side of the occipital lobe, one would have seen examples of fairly definite localization of function. It is, moreover, my impression that since he has been working with higher animals Professor Lashley has modified the earlier views which he expressed on the basis of experiments on rats.

These are all minor theoretic points. This is, as far as I know, the first time that basal nuclei have been deliberately extirpated surgically, and any account of

the physiology of the basal nuclei will have to take this operation into account. So will every future surgical attempt at the treatment of alternating tremor.

DR. JOSEPH E. J. KING: I wish to congratulate Dr. Meyers on this unusual procedure and on his results. It is a marvelous operation, as demonstrated by the 3 cases reported. One of the most interesting points about the operation is its origin. I understand that Dr. Browder obtained the idea from a case in which he did lobectomy and carried the extirpation down rather far into the caudate nucleus. Before operation the patient had trembling limbs and the facies observed in Parkinson's disease. After the operation Dr. Browder, with his usual powers of observation, noticed that the shaking had stopped and the facies cleared. This observation led him to the conclusions which resulted in the operation described tonight.

It is to be hoped that none of my colleagues will attempt this operation—I am sure that I shall not—until Dr. Browder and Dr. Meyers tell us to go ahead. It is a splendid operation, and I think that we should wait, watch and learn until they are satisfied with their own results; otherwise, the operation may fall into disrepute as a result of being improperly done or carried out for the wrong condition.

DR. S. PHILIP GOODHART: The extraordinary results obtained with this new surgical approach for relief of a distressing symptom prompts me to ask if there is any hope for a similar approach in cases of dystonia musculorum deformans. No more disabled group of patients seek help than the young people with static and kinetic forms of dystonia, for which the means of relief are so limited. The bold, yet carefully sought, plan of the surgical approach, so ably carried out, and its technic, so clearly demonstrated in tonight's presentation, appeal to those who have seen surgical methods vainly applied in cases of dystonia. At Montefiore Hospital there are various forms of extrapyramidal syndromes. In an occasional case of postencephalitic dystonia the prolonged application of plaster casts has proved successful in improving the posture, adaptation and control. A direct surgical attack on the pathologic area or the mechanism of its influence in basal ganglion disease has been the ideal of those who have dealt with the problem. Surgical treatment, based on concepts of physiologic function and applied to extrapyramidal lesions, has often proved disappointing. I may mention the case of a girl now at the Montefiore Hospital. She had generalized kinetic dystonia and was originally operated on about five years ago; at that time partial cervical chordotomy with section of the lateral column was done, and the anterior and posterior roots of the second, third and fourth cervical nerves were crushed. Little impression was made on the dystonic movements, and only temporary paresis and anesthesia resulted. A few years later she was again operated on; at this time, as I recall, both spinal accessory nerves were resected, and the second, third and fourth cervical roots, anterior and posterior, were cut. Practically no influence on the dystonoic movements resulted, although partial atrophy of muscles followed.

The sympathetic system may play a greater role in certain conditions than has heretofore been assumed, and pathologic changes may affect functional and anatomic relationships.

The intricate problems that face the neurologist in the large realm of basal ganglion disease may find their only solution in such striking and painstaking studies, with the applied technic, as those demonstrated tonight.

DR. JOHN E. SCARFF: I should not like the occasion to pass without adding my tribute to Dr. Meyers' surgical imagination, courage and skill. I congratulate him on his fine achievement. This is one of the most provocative, and possibly one of the most valuable, papers that this society has had the privilege of hearing, and I am sure I express the gratitude of all the members to Dr. Meyers for allowing them to enjoy his presentation of the subject at this time.

DR. H. RUSSELL MEYERS, Brooklyn: Your very kind reception is more than I could have hoped for. I wish particularly to thank Dr. Putnam, Dr. King, Dr. Goodhart and Dr. Scarff. I agree with Dr. Putnam wholeheartedly that the

questions raised by present physiologic considerations are much more numerous than one is able to answer, and the theoretic inquiries will certainly have to be reserved for future demonstrations of the validity, if any, of this procedure.

Dr. Goodhart inquired concerning the possible application of the procedure to the dystonias. It has already been suggested to the neurosurgical staff in the Brooklyn Hospital that it be carried out. My inclination, however, has been for the time being to reserve the operation for the problem in hand and not to confuse the issue by operating on patients with physiopathologic conditions which may have a wholly different origin than have tremors at rest. It may be that the future will enable one to turn attention to the problem of dystonias, but it must be in the future.

Clinical Syndrome of Occlusion of Rolandic Veins. DR. HAROLD R. MERWARTH, Brooklyn.

Sudden obstruction of the circulation of the superior longitudinal sinus, either from acute infectious involvement or surgical removal of a portion of the sinus, previously unoccluded, has serious sequelae. Acute purulent thrombophlebitis of this sinus is accompanied by extension into the tributary superior cerebral veins, with severe secondary changes in the gray and adjacent white matter varying from minute to large extracerebral and intracerebral hemorrhages or multiple abscess formation. Similar hemorrhagic changes of varying severity may be precipitated by ill considered surgical interruption of an unobstructed sinus at or behind the rolandic point for removal of a tumor.

Gradual occlusion of the sinus, on the other hand, whether produced by tumor or retrograde thrombosis, is compatible with life and the absence of focal signs. Successful resection of this sinus at or behind the rolandic point has been reported by David and his co-workers, Rose, Adson and Maltby. In each instance in which verification was made by histologic examination the resected sinus was found to be occluded by tumor. The slowness of the occlusion of the sinus by tumor and the extent and efficiency of the collateral circulation of the cerebral veins are important determining factors permitting section of the sinus. The same factors operate in slowly progressive non-neoplastic thrombotic obstruction of the sinus when focal signs are not produced (otitic hydrocephalus).

Sudden severe interruption of the venous current in the longitudinal sinus causes flooding of the tributary superior cerebral veins, with circulatory stasis and production of focal symptoms. Also, if the circulation within a superior cerebral vein is primarily obstructed by tumor or infection, clinical signs with precise characteristics may be produced.

The flow of blood from the cerebral veins is in two directions; that from the superior cerebral veins is upward toward the sinus, represented roughly by a horizontal line drawn through the tip of the sylvian fissure. This tends to spare the face areas in the rolandic strip and the speech areas in the temporal lobe. The lower half drains into the middle cerebral vein and thence into the cavernous sinus. There is an elaborate, rich, free anastomosis between the veins in the superior group. Also, a rather free connection between the upper and the lower group is made by way of the anastomotic vein of Trolard.

Latent anatomic factors leading to ready thrombosis or spread of thrombosis from the longitudinal sinus are: (1) total absence of valves in the superior cerebral veins; (2) low venous pressure; (3) flow of current in the middle and posterior veins against the current in the sinus, due to the angle of entrance into the sinus; (4) ready reversibility of current on coughing, sneezing or straining.

In addition to the aforementioned factors, the surgical use of electrocauterization, with the production of heat leading to clot formation, is of importance in dealing with the surgical occlusion of veins as they are about to enter the sagittal sinus.

Few observations have been reported in which isolated primary obstruction of the rolandic veins has been associated with contralateral signs and symptoms.

However, cases have been reported by Gowers, Dusch, Dowman, Lannois, Wagonner and Davis. The real concept of involvement of the superior cerebral rolandic veins was postulated by Holmes and Sargent. It consisted of paralysis, of unusual distribution and type, early muscular rigidity and disturbance of sensation essentially cortical in type. Facial paralysis was uncommon. Speech was not affected.

The following 3 cases illustrate a syndrome of involvement of the superior cerebral rolandic veins.

REPORT OF CASES

CASE 1.—A woman aged 50 suffered from convulsive seizures. The results of physical examination were normal. At operation, performed because of positive encephalographic findings, a parasagittal meningioma was observed posterior to the rolandic point. Several large veins were occluded during its removal.

The patient was right handed. Disturbances of speech or facial paralysis did not follow the operation. After the operation right hemiplegia was present. There was early recovery of motion in the fingers and hand, which followed the cellular pattern of the rolandic strip, improvement appearing successively in the elbow, shoulder, hip and knee, and lastly the foot. Sensory disturbances of the gnostic type were found. Marked early plastic hypertonicity was observed. The patient continues well, except for spastic involvement of the right foot.

CASE 2.—A woman aged 54, who was right handed, was operated on for a condition diagnosed preoperatively as left parasagittal meningioma and venous thrombosis of the superior cerebral rolandic veins. There was no facial paralysis and no defect in speech. The right arm and leg were paralyzed. The paralysis spared the movements of the hand and finger, but there was complete weakness of the elbow, shoulder and leg on the right side, with signs of pyramidal involvement. All modalities of sensation were involved, but discriminative types most. After the operation the patient made a recovery which again followed the cellular pattern in the rolandic strip.

CASE 3.—A woman aged 62 had "sensory hemiplegia," and air studies suggested a neoplasm in the right posterior region. Motor paralysis followed the operation. Recovery again followed the motor pattern of the rolandic strip, beginning in the fingers and hand and slowly spreading to the elbow, shoulder and down the leg. The foot was the last to improve.

The cerebral veins can be viewed as a system of veins or rivers, each possessing a variable number of tributaries. They differ from rivers, however, in the anastomoses with each other, which exist in a varying degree. The superior longitudinal sinus may be viewed as the ocean into which the upper set of rivers finally discharges.

If a severe obstruction occurs at the mouth of the river just as it is about to enter the sagittal sinus, damming up occurs in the tissues which it drains. If the flooding of the tissues is severe, clinical symptoms will result. If the collateral circulation is able to handle the increased load, little disturbance will be caused.

It is when the superior cerebral veins are interfered with at the point of entrance into the superior longitudinal sinus that more serious complications arise. There is no possible outlet at this point and the outflow must be taken care of by other channels. Thus, there results more serious occlusion when there is suppuration in the sinus, when the cerebral veins are ligated close to the sinus and, finally, when the drainage is impaired, as in the case of a tumor immediately adjacent to the sinus.

In the 3 cases reported the outstanding feature was the mode of recovery of motor function, which followed the cellular pattern in the rolandic strip, namely, up the arm and down the leg. There was early recovery of function and power in the fingers and hand grip, followed in turn by recovery of the elbow, shoulder, hip and knee, and lastly the foot. Facial paralysis was not present. There was no disorder of speech, 2 of the patients being right handed and having right hemiplegia.

Spasticity had an early onset, appearing immediately in 1 case and within three days in the second. Loss of sensation was mainly in the gnostic fields, although pain sensation was also slightly diminished.

DISCUSSION

Dr. Tracy J. Putnam: I am particularly gratified to have the cortical veins recognized as functional structures. Vascular accidents have long been regarded as synonymous with arterial occlusion; indeed, to read some textbooks of neurology one would imagine that the capillaries and veins were placed in the brain simply for ornament. Having done a little work in this field, I have come to have the impression that venous thromboses are far more common than arterial thromboses in the brain. This is recognized by general pathologists and hematologists to be true of thromboses in small vessels elsewhere in the body, in part because the current is slow in the veins, and perhaps in part because the blood contains more carbon dioxide. As a result of venous thrombosis there is ordinarily a relatively widespread, mild degenerative process, as contrasted with relatively localized necrosis produced by arterial lesions. It is striking that the degeneration produced by the cortical venous thrombosis, either experimental or pathologic, may be confined to the cortex or to the white matter. Of course, thrombosis of many veins can lead to as complete necrosis as an arterial closure, but a larger stretch of vein must be occluded. Dr. Merwarth has well illustrated his point in regard to the cases which he has reported, and I feel sure the process is as he has described it. I should raise the question, however, whether a single ligation of a vein necessarily has as serious an effect as his closing remarks would indicate. It is my impression that the network over the surface of the brain has sufficient anastomosis to permit recovery from closure at a single point, whereas if a long length of vein is occluded all the tributaries running into that portion become obstructed, and severe infarction is likely to result.

I cannot help throwing in one remark. Thrombosis of veins, even in the cortex, brings about degeneration affecting chiefly the myelin sheaths and leaving the axis-cylinders in the white matter intact. In Dr. Merwarth's paper was the report of a case by Dr. C. E. Dowman, of Atlanta, Ga., in which thrombosis of the cortical vein was observed on exploratory operation. I heard of this patient subsequently from Dr. Fincher, and learned that he recovered from the hemiplegia but presented other disseminated lesions elsewhere in the nervous system.

Dr. John E. Scarff: I have ligated the superior anatomosing veins at their junction with the superior longitudinal sinus in 28 cases. In 3, ligation was subsequently carried out on the second side, making 31 ligations altogether. These were all done on epileptic persons with clinical evidence of epileptogenic foci at the superior mesial border of the cerebral hemisphere. None of the patients had expanding lesions.

One patient died as a result of the ligation. In this case the vessels were arteriosclerotic, and there was a spontaneous intracortical hemorrhage immediately after ligation. The patient never recovered consciousness. One infant died during the course of too rapid transfusion following the operation, after she had left the operating room. Death in this instance appeared to be due to congestive failure of the right side of the heart.

In 25 of the remaining 29 cases of unilateral ligation of the superior anastomosing veins, no untoward symptoms or signs of any sort were shown during the postoperative period. Of the 4 in which there were signs, right hemiparesis associated with aphasia was present in 3 and left hemiparesis in 1. These signs and symptoms developed within the first twenty-four hours, and came to complete fulfilment within forty-eight or seventy-two hours; in each instance they had completely disappeared before two weeks had passed. In only 1 case were the day by day descriptions of the paresis really detailed, but in this 1 case it is clear that the upper and lower extremities became involved at the same time, that the

upper extremity was more affected than the lower and that the more distal muscle groups of both the lower and the upper extremities were more severely injured than the proximal.

That some patients have paresis after ligation of the superior anastomosing veins and some do not depends on the adequacy and speed with which collateral circulation develops in the venous system. There is great variation in the anastomosis of the larger cerebral veins; I shall show two or three slides to illustrate that point. In one slide, for example, the veins are practically of equal caliber throughout their course, from the superior longitudinal sinus to the sylvian veins. They are able to drain in either direction. On the other hand, the second slide from another case shows superior anastomosing veins which are much smaller in caliber and which appear to be lost long before the sylvian veins are reached. Apparently, in the second case there is no free, or at least gross, communication between the superior longitudinal sinus and the sylvian vein. The third slide shows a block of about 2 to 3 cm. of the superior longitudinal sinus which was resected during removal of a bilateral parasagittal meningioma, situated near the rolandic fissure. The normal drainage from all the superior anastomosing veins anterior to that point was completely stopped in this case, but the patient had no disturbances after ligation and removal of this portion of the sinus. However, an important point to be noted is that the sinus at this point was found to have been invaded, and completely filled, by tumor tissue; this must have taken place gradually. Under these conditions there was time for the collateral circulation to develop as needed. Compare this with a similar tumor in another case in which operation was performed a few weeks later. At this operation the sinus was also resected. The second patient presented extreme symptoms of involvement of the frontal lobe, became quadriplegic and died. Unfortunately, it was not possible to secure permission for autopsy, so it cannot be stated exactly what changes took place in the brain after ligation of the sinus. I know, however, that the sinus at the time of ligature was patent and was transmitting an adequate volume of venous blood. The demand for establishment of a new collateral circulation was therefore immediate and abrupt, and it would appear that this demand was too sudden to be met adequately.

These various observations seem to indicate that there is a collateral venous circulation of the cerebral cortex which is not normally used, and which is capable of taking over completely, in most instances, the work of the superior anastomosing veins. Time, it appears, however, is an important factor in its effective development and functioning.

DR. HAROLD R. MERWARTH, Brooklyn: I cannot answer Dr. Putnam's question whether ligation of a single vein will produce symptoms. I have not had any experience with that particular phase of the problem. Waggoner's work, which I cited, is such an example of occlusion of a single vein (Thrombosis of a Superior Cerebral Vein: Clinical and Pathologic Study of a Case, ARCH. NEUROL. & PSYCHIAT. **20**:580 [Sept.] 1928). I attempted to emphasize that the appearance of symptoms depends largely on the anastomoses that are available and the abruptness of interruption—a point which Dr. Scarff has also emphasized and which has been stressed by practically all writers in this field, particularly when the superior sagittal sinus is interrupted. If the occlusion is slow no symptoms will be produced. I venture to say that in the case mentioned by Dr. Scarff in which the patient died the pathologic features were similar to those in the case in which two superior cerebral veins of the anterior group were occluded. The number of veins in the rolandic area varies considerably, from one to four. They anastomose elaborately. Dr. Browder has observed some of these veins dilate at operation when the adjacent veins have been electrocoagulated. It seems to me that in production of the so-called venous syndrome occlusion is not as necessary as temporary stasis. That partially answers Dr. Putnam's question—the ultimate picture depends on the efficacy of the collateral circulation.

ILLINOIS PSYCHIATRIC SOCIETY

H. DOUGLAS SINGER, M.D., *President, in the Chair*

Regular Meeting, March 7, 1940

Effect of Very High Temperatures on the Brain of Man and Animals. DR. NORMAN B. DOBIN, Chicago.

Fifty-seven animals were each subjected to one treatment with artificial fever. Frozen carbon dioxide was packed around the neck. The temperature was elevated to 110 F. Temperatures above 107 F. were maintained for from sixty to eighty minutes. The brains of 18 animals were studied. Seven were from animals that lived for five months after the experiment.

The brains of the animals that died during or shortly after treatment showed hyperemia, maximal dilatation of the blood vessels, hyperleukocytosis, perivascular edema and hemorrhages, acute changes in the ganglion cells and swelling of the myelin sheaths and nerve fibers. The brains of the surviving animals showed changes in the ganglion cells, neuronophagia, marked increase in glia cells, organization of old hemorrhages and demyelination about areas of former perivascular hemorrhage.

A white woman aged 52, with advanced inoperable carcinoma of the bowel, was subjected to fever therapy. Her body temperature was maintained at from 106 to 107 F. for about two hours, and at 107.8 F. for sixty minutes. Microscopic studies of the brain revealed hyperemia and edema along the medium and large blood vessels.

DISCUSSION

DR. ARTHUR WEIL, Chicago: It seems that the threshold of safety for the nervous system is much narrower for higher temperatures than for lower ones. Demonstrations of the latter were furnished at the annual meeting of the American Medical Association, in 1939, at St. Louis, where one saw the whole human body exposed to temperatures near the freezing point. On the other hand, the human body cannot tolerate a temperature of 43 C. (109 F.) without being severely damaged, and the highest temperature observed with survival is 44 C. (111 F.). In evaluating the effect of higher temperatures on the central nervous system, one should differentiate between the direct effect of the heat and the indirect effect produced by changes in the body fluids and in other organs of the body. The dogs in the present experiments had been submitted to temperatures as high as 110 F. They were killed immediately, and their brains showed severe histopathologic changes.

The question arises whether these changes are transitory and whether the therapeutic results justify subjecting the human body to such high temperatures, at the risk of serious damage. It seems to me that there remains lasting damage of the central nervous system, as judged from the study of preparations from dogs which survived and were killed after several weeks. Many neurons broke down completely; the hemorrhages which had occurred left glial scars and areas of demyelination. Again the question arises: Can one compare this type of experiment with the ordinary course of fever therapy? From practical experience one may say that the danger limit is from about 105.5 to 106 F. One must also take into consideration the general condition of the patient. The aged and arteriosclerotic patient will be more susceptible than the younger patient; the cachectic one, more than one in a state of good nutrition.

Dr. Neymann's idea was to keep the temperature of the brain down to normal levels. Though he succeeded in lowering it 2 degrees F., he could not eliminate the pathologic changes produced in the body fluids and in the other organs of the body. There were increased leukocytosis, hemolysis and stasis of circulation in the brain. Of course, these changes interfered severely with the nutrition of the

ganglion cells of the cerebral cortex, which cannot stand more than ten minutes of complete lack of oxygen without serious damage.

In summary, one may say that, though the author succeeded in keeping the temperature of the brain below that of the rest of the body, this temperature was still too high and caused injury of the vascular endothelium, hemorrhages and disease of neurons. Also, there was the damaging influence of the pathologic change in the body fluids brought about by high temperature in the rest of the body. However, I do not wish to create the impression that on the basis of the histologic changes in such laboratory experiments, the pathologist should object altogether to such treatment. I assume that the authors were conscious of the danger line of 106 F. in their experiments on patients.

It is remarkable how the protoplasm of the living body can adapt itself to changes in temperature. In Dr. Ranson's laboratory, experiments were carried out in which the heat-regulating centers were destroyed by electrocoagulation. The animals became poikilothermic and adapted themselves to the temperature of their environment. However, if they were kept for several days in the cold box preceding this operation, they were able to sustain their body temperatures at higher levels than other animals which had been kept at the temperature of the environment but had not been placed in the cold box before operation. One might suggest that it should be possible by gradually adapting patients to higher temperatures to extend the danger limit of 106 F., and thus to use such higher temperatures therapeutically, with less risk of damage to the central nervous system.

Dr. Peter Bassoe, Chicago: I wish to ask whether any disorders in motility were observed in the dogs that lived four or five months. In the literature concerning sunstroke, there are reports of states resembling multiple sclerosis in human beings who had had extremely high temperatures. I remember a man who worked in a trench on a very hot day. He presented a condition that aroused much comment, some claiming it was multiple sclerosis, because the man had been healthy before, and others that it was due to the heat. I found a number of reports of this kind.

I wish also to ask how these changes compare with those described in cases of ordinary sunstroke.

Dr. J. A. Luhan, Chicago: It has long been known that some of the conventional designations or pathologic diagnoses of the several forms of ganglion cell disease are misnomers. It was interesting to see here, in cases of death due to hyperpyrexia, typical changes that one is accustomed to call chronic ganglion cell disease, with shrinkage, pyknosis and corkscrew forms of the main dendrites appearing in the acute preparations.

Dr. Clarence A. Neymann, Chicago: If Dr. Bassoe will permit, I will answer the question as to the changes in the motility of the dogs. The dogs which died all had acute symptoms; all died in convulsions, some in states that might be compared with decerebrate rigidity.

Dr. Norman B. Dobin, Chicago: No disturbances of motility were elicited in the animals that lived after the experiments. These animals had good motor control of the limbs, trunk, head and tail.

The changes in the brain associated with sunstroke have been described in the literature. The lesions reported are those resembling the so-called acute cell disease of Nissl, perivascular edema and small perivascular hemorrhages.

Psychologic Tests of Schizoid and Cycloid Reactions. Dr. G. K. Yacorzynski, Chicago.

Perceptual, emotional, preferential and other responses of manic, schizophrenic and control subjects were measured by various methods. The present report deals with: (1) the "introversion-extroversion" questionnaire; (2) incompatibility of motives; (3) perceptual configurations in the completion of figures, and (4) preference for temporal patterns.

The results point to the following conclusions: 1. The differences between the manic-depressive and the schizophrenic patients in answers to an introversion-extroversion questionnaire cannot be accounted for on the assumption that the questions are a measure of a single trait; such a test seems, rather, to measure a number of factors. 2. Both psychotic groups show a greater incompatibility between desire and action than the controls. The situations producing these "tensions" appear to be related for the two psychotic groups. 3. Differences in the completion of figures which the manic patients display can be accounted for on the basis of greater expenditure of energy. The schizophrenic patients tend to use less energy in the completion of figures, but part of the differences which this group shows seems to be dependent on other factors, such as the patterning of stimuli. 5. The control subjects display the same preference for nonsymmetric temporal patterns as the general population, reported by Goodfellow (*J. Exper. Psychol.* **23**:601-632, 1938). This is not true of the two psychotic groups, although their preferences appear to be related.

DISCUSSION

DR. DAVID SLIGHT, Chicago: The differentiation of the manic-depressive psychoses and the schizophrenias has long been a problem; any effort such as the present study is commendable. It may be that such research will break down the clinical differentiations held by some investigators and substantiate the idea that the conditions are often more closely allied than present nosology implies. With regard to "psychologic" tests, I think one must distinguish between tests that are more purely psychologic, that is, those which reveal the psychologic organization, and tests which may well be called psychologic but concern rather general physiologic functions.

In his summary of the results of the second and third tests, the author mentioned failure or weakness of executive capacity as compared with desire, and the greater or lesser expenditure of energy indicated by the results. This suggests that he was measuring general physiologic capacity rather than psychologic capacities as such. Or, to put it in another way, one may distinguish between quantitative factors and qualitative differences, such as were elicited in the questionnaire method. The choice of tests to be used is a problem in itself, and I have no doubt that the author was ruled by special indications as to the choice of the present tests, as compared with others now popular. It is evident that he has shown differences between the control group and the psychotic groups, although few differences are apparent between the two psychotic groups. Personally, I am not sanguine about the possibility of determining by psychologic tests essential differences between many of the patients classified in the two groups. However, one hopes to develop tests which will show at least trends of deviation. In so many cases of functional psychoses the differences seem those of degree and not of kind. It may be that in some cases of schizophrenia studied the results of the tests were such as to approach those obtained generally in the manic-depressive group. If that was so, I should be interested to know whether there was any opportunity to check the clinical diagnosis for the differential value of the psychologic tests. The author is to be commended on an elaborate and painstaking study, which represents a worth while effort in psychiatric research.

DR. SAMUEL J. BECK, Chicago: I shall open my discussion by raising two questions, which are not original with me, but which I have not seen answered in the literature. There are at least two fallacies in the questionnaire method. One might be called its automatic self-blocking property. A patient comes to a psychiatrist; the questionnaire is presented to him, and it stirs up some of the very emotions which made him come for treatment. The patient is on the defensive, which is natural. One is asking him to testify against himself. Furthermore, the more important the emotional factor the stronger the block, and what one most wants to know about may be most strongly blocked. I may be mistaken in this, but I should like the objection answered.

The second fallacy is that while the answer represents ostensibly what the patient does under the circumstances which the questionnaire sets, there is grave doubt as to whether it tells what he would really do. The chances are that to the question: "Are you always calm and collected?" the answer will be a wish fulfilment. So what one secures is not so much a representation of what the patient is, but what he thinks he is or would like to be. This really becomes an expanded intelligence test. Whether one would do a certain thing under certain circumstances is a question, on the one hand, of ambition and, on the other, of the influence of actuality. The discrepancy between the two is often wide.

To come to the experiments of Dr. Yacorzynski: I think his first conclusion supports the view I have just presented with regard to the fallacy of the questionnaire method; he found that of twenty-one questions concerned with extroversion certain criteria were met by only six. The conclusion is that the introversion-extroversion test can be assumed to be a measure not of a single trait but of a number of factors. I can accept that, but I should add that failure to meet the criteria shows the inadequacy of this method in differentiating the groups of subjects.

The next topic, incompatibility of motives, appears to be a sort of by-product—and a valuable one—of the experiment. I wish to ask Dr. Yacorzynski what he means by the question: "What did you have to do under the circumstances?" Was he asking the patient whether he had a compulsion to do the thing? Did the patient think he had a compulsive need? If the patient could answer that he would not be a patient. He does not know why he behaves as he does.

As to statistics, they show significant differences, but statistics are only as valuable as the investigation which they represent.

The last experiment, I think, has possibilities of real progress. It follows some of the work done in the Bellevue Hospital by Dr. Bender and Dr. Schilder, and is typical of the approach by which one does not ask the patient any questions but gives him something to do, of which he leaves a record. One can compare the response of the manic and the schizophrenic patients with that of the controls, can work out a pattern and can distinguish one from the other. For example, the schizophrenic patient in drawing a window does something that he does in every test, and that differentiates him. He draws *different* windows. He is a nonconformist in everything. I hope this particular experiment will be carried much further.

Dr. G. K. Yacorzynski, Chicago: Dr. Slight asked whether I checked the clinical diagnosis with the results of the tests. I have not done this because I have not yet compiled all the results of the tests. After all the data are compiled, it may be possible to say what relationships exist, not only in the different groups of psychotic persons, taken individually, but also in the test results. I am not interested so much, from my own standpoint, in compiling a test for the differentiation of manic-depressive and schizophrenic persons. If such differences exist they should be shown by these tests; if not, one must accept the results as one obtains them. My interest lies rather in studying what differences in reactions in personality exist between the various classifications of psychotic and normal persons. Since there is such a great shift in the personality of the psychotic patient from that of the average normal person, one may assume that whatever changes take place are of fundamental nature in the personality makeup. Thus, one has a method of studying the important factors of the personality of normal persons.

In the gestalt completion test, I found that the only difference between the manic-depressive and the control or the schizophrenic persons was in the expenditure of energy, which is a physiologic rather than a psychologic factor. It is my impression, however, that if one had technics fine enough for measurement, a physiologic counterpart could be found for most of the psychologic factors.

In work of this kind, in which comparatively new tests are used, there is always a tendency to pay a great deal of attention to terms and to demand definition of terms beyond the strict meaning or description based on the experimental

results. I think, for example, that part of Dr. Beck's criticisms, or the questions which he raised, depend not on actual disagreement with what I have said but on differences in the use of terms. We both agree on the inadequacy of the questionnaire method in measuring introversion and extroversion, but my criticism is based on the experimental data. One of the objections which he raised was the "self blocking" which might be obtained if one asked the subject questions that were emotionally toned. Of course, that does enter in and is a just criticism of the questionnaire method. For that reason, an attempt is always made to select questions which do not have a great deal of emotional tone, so as to minimize the possibility of emotional blocking or rationalization.

Another objection was the possibility that the subject answered the questions with "wish fulfilment." In asking the questions one wanted the subject to state what he actually wished or desired to do and not what he was more often required to do. Dr. Beck stated, wrongly I believe, that the questionnaire tests of personality are actually tests of intelligence. So far as I can recall, the majority of correlations reported in the literature between personality and intelligence have approximated zero. In addition to the objection to the introversion-extroversion test raised in the paper, which was simply an interpretation of the results of the experiment, other grounds of criticism of the introversion-extroversion classification have been furnished by different experimenters. The introversion-extroversion concept has probably little value as such, but sometimes tests, such as those of intelligence, which measure a number of variables are of value for practical clinical purposes.

Dr. Beck wanted more information on the part of the experiment in which I attempted to measure what the person desires to do as compared with what he actually has to do. First, I wanted to know whether the subject liked the idea which the question expressed. This was stated in the instructions, and each question was preceded by the statement: "Do you like the idea ——?" In the retest I instructed the subject to state what he had to do usually in the situation described by the question, and preceded each question by the statement: "Do you ordinarily ——?," or "Are you ordinarily ——?" This procedure showed a difference between the psychotic and the control subjects which could not be explained on the basis of the unreliability of the method. I do not care what this difference is called. It is, however, a differentiating characteristic.

The last question raised was whether I used exclusively patients with either a manic or a depressive state, or a mixture of the two. In the different groups of subjects submitted to these tests there were always a number which could be classified as being in the manic, in the depressed or in the normal state. I do not recall the exact percentages in each of the groups of subjects used.

Borderland Between Schizophrenias and Manic-Depressive Psychoses. Dr. Clarence A. Neymann, Chicago.

Clinical investigation of 27 patients suffering from mixed types of functional psychoses approximating the syndromes of manic-depressive psychosis and schizophrenia was undertaken. It was found that at least 60 per cent of the patients had recovered and returned to their former occupations after two years. It also appeared probable that the psychoses did not have the same tendency to recur as outspoken cyclic forms of manic-depressive psychosis.

It was assumed, therefore, that some unknown factor stimulates recovery in these types. The use of the Neymann-Kohlstedt and Rorschach tests did not give an insight into the basic psychologic patterns. In fact, the results of both tests were not at all in agreement with the clinical diagnoses. The clinical diagnoses changed from time to time, depending on the changes in the patients' attitudes and the viewpoints of the examining physicians.

It is suggested, therefore, that the entire concept of manic-depressive psychosis and schizophrenia should be interpreted with less rigor. The two diseases certainly

merge into one another in the borderland, and in some cases schizophrenia approximates the clinical concept of a severe psychasthenia.

It is my belief that attempts to classify individual reactions and to pigeonhole cases have resulted in a constantly changing nomenclature. This is valueless until the underlying causes of mental illness are known. A descriptive terminology, such as existed before these syndromes were crystallized around preconceived artificial central psychologic cores, is therefore more practical than the present custom of rigid sorting.

Moreover, if hundreds of persons in the population at large are examined by means of personality tests, a smooth curve results. This shows that in large groups cyclothymic traits imperceptibly merge into schizophrenic attitudes. There is every reason to suppose that the same factors apply to psychotic persons, who probably reflect this mass psychology in a distorted individualistic manner.

DISCUSSION

Dr. H. Douglas Singer, Chicago: I am interested in this report because it shows the confusion between study of the patient and study of the sickness. Dr. Neymann emphasized the dangers incident to the incorrect use of words. One such word that is used freely is "diagnosis"; the word means "knowing through and through." What does one know thoroughly about the patient? Yet one makes a diagnosis. The names used apply to the personality of the patient and not to his illness. As long as one confuses the two issues there cannot be a diagnosis. Types of personality show a curve of frequency, with a few definite extroverts at one end and a few definite introverts at the other, but with the great majority between. If one charts the forms of the psychoses one finds a similar distribution, with a few strikingly cyclothymic and a few definitely schizophrenic types at either end, but the greater number in the middle. This does not mean that the kind of illness is different.

Kraepelin performed a real service, although possibly too much emphasis was placed on the prognostic phase. Still, he established that there are at least two kinds of illness, one most often reversible, the other not reversible. However, one is not justified in concluding that because one observes formal symptoms the disease is of deteriorating nature. I failed to see evidence of a schizophrenic reaction in the patient whose case was described. It was said that he looked as if he was listening to voices; I do not consider that good evidence. It is too easy to say that certain formal symptoms, such as hallucinations, indicate schizophrenia. To me the important indication is the use of symbolized thoughts, words and acts to hide the real meaning.

The chief point I wish to make is that one should not confuse the issue between the nature of the illness, which will determine a certain course, and the form of the reaction, which belongs to the personality of the patient.

Dr. V. G. Urse, Chicago: I have had a great deal of contact with the patients Dr. Neymann studied, and since his work was completed Dr. Gerty, Dr. Meduna and I have made some biochemical studies in cases of schizophrenia. Our work was concerned primarily with pure outspoken schizophrenia, but in the course of studying 36 or 37 patients we came on 2 with pictures of depression as well. The condition was of such nature that I am reasonably sure that if the patient had been examined from day to day, and if different examiners had seen them, it would have been classified by some as schizophrenia and by others as depression. We found that changes characteristic of all the schizophrenias, pure and simple were not present in these 2 cases. Although the number is so small, I think it important to bring out that something which exists in the schizophrenic person was lacking here.

Dr. Clarence A. Neymann, Chicago: I wish to say to Dr. Singer that I heartily agree with him. In my opinion, the patient whose history was summarized was not schizophrenic. He was not presented as a manic-depressive person. He

was presented only as having a recurrent psychosis, the pathologic and dynamic character of which is unknown. The point is that the patient had recurrent attacks from which he recovered. During the periods in which he was ill he was examined by various specialists. They disagreed on the diagnosis. In this case, as in the others, no definite diagnosis was apparent. If I hinted that the patient seemed more schizophrenic than manic, or vice versa, this was only a reflection of my attitude—a parlance, a way of speaking. Psychiatrists have arranged mental states around central psychologic cores. In the middle of the clusters there are certain types, all of which will be diagnosed immediately and readily. At the periphery, the clusters merge into one another. Conditions corresponding to pure types are therefore comparatively rare. In general, the psychoses and neuroses reflect the psychologic trends of the population at large. Normal persons vary among themselves, but when large numbers are examined their types merge into one another. The same facts apply to psychotic and neurotic patients. In disagreeing with a diagnosis that was not made, Dr. Singer has confirmed this premise.

NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY, AND NEW YORK NEUROLOGICAL SOCIETY

LEWIS D. STEVENSON, M.D., *Chairman of the Section, Presiding*

Joint Meeting, March 12, 1940

Supratentorial Hemangioma with Hemorrhage: Presentation of Two Cases. DR. IRA COHEN.

In their monograph entitled "Tumors Arising from the Blood Vessels of the Brain," published in 1928, Cushing and Bailey expressed skepticism about the occurrence of true angioblastic tumors above the tentorium. In the volume reporting 2,000 verified intracranial tumors, published in 1932, Cushing did not include such a lesion.

I present the cases of 2 patients who have been operated on for hemangioma of the cerebrum. In the woman the lesion was in the left parietal region; in the man, in the right frontal region. The presenting symptoms were focal convulsions in both instances. The duration of the illness before entrance to the hospital was less than a week. In each instance old fluid and clotted blood were found beneath the cortex. Histologic study of the excised tissue revealed a hemangioma.

I have observed a third case, similar in every respect, even to the hemorrhage.

From my experience I conclude that true angioblastic neoplasms may occur above the tentorium. They seem to show a greater tendency to hemorrhage than similar lesions in the posterior fossa. In all but 3 cases convulsions were noted. The postoperative prognosis is good.

DISCUSSION

DR. JOSEPH E. J. KING: All are indebted to Dr. Cohen for his account of these 2 cases, and he is to be congratulated on his splendid results. The cases are answers to the facetious remarks frequently directed toward the neurosurgeon and his results. The first patient looks as though she had never been ill in her life and the man looks well.

I do not know that I have ever operated in a case of hemangioblastoma of the cerebral region. I had thought that hemangioblastoma was usually associated with the cerebellum; now Dr. Cohen has reported 2 cases of the cerebral type, in both of which operation gave fine results.

DR. J. H. GLOBUS: The 2 cases presented by Dr. Cohen are of significance for several reasons. First, they draw attention to the fact that hemangiomas, which until recently were regarded as lesions almost always restricted to the cerebellum, are not infrequent in the supratentorial region. Although Dr. Cohen reports only 2 cases at this time, there is a much larger number of instances in which hemangiomatous lesions have been observed in the cerebral hemispheres.

Again, this presentation raises the question of the classification of a lesion of this type. Should it be regarded as an anomalous formation of blood vessels, or should it be placed in the category of cerebral neoplasms? Since it is an expanding lesion and, in all probability, gains in size as time progresses there is every reason to accept it as a tumor. This is supported by the observation that hemangiomatous tumors display gradations in histologic makeup. On the one hand are the vascular tumors, made up of mature, well defined and inactive blood vessels, as seen histologically, which suggests that their character is that of an anomalous vascular formation; on the other are tumors in which the cellular structure is that of an aggregation of immature capillaries, consisting primarily of endothelial buds. The former is designated as hemangioma, the latter as hemangioendothelioma. As these hemangiomatous tumors may present a low grade of differentiation, on the one hand, and advanced maturity on the other, it is reasonable to assume that one is dealing with stages of neoplastic formation. Hence, for a large number of tumors of the hemangiomatous variety a neoplastic origin may be accepted, and to distinguish between the mature and the less differentiated hemangioma it is advisable to name the former hemangioma and the latter hemangioendothelioma. Essentially they are meningiomatous growths.

I shall discuss also the occurrence of bleeding in such tumors. Certainly, in the hemangiomas, which contain large vascular channels filled with stagnant blood, the surgeon on inserting his exploratory needle will often encounter blood; since many hemangiomas consist of large venous channels, the blood may be dark and the surgeon may be led to assume that he has entered an area of old hemorrhage. Even when material of this type is submitted for histologic study and the pathologist discovers large extravasations of red cells and many macrophages containing pigment of laked blood, the assumption of hemorrhage into the tumor resulting from external force or violence need not be made. Any one who has studied a large series of tumors of the brain, particularly such as are rich in blood vessels, knows that even in the most quiescent state and under conditions in which the tumor has not been subjected to violence many blood cells may be found outside the blood vessels. Pigment also may be seen in macrophages about blood vessels or in areas in which larger accumulations of blood occur. Therefore, great caution should be exercised in interpreting accumulations of red blood cells within a tumor and the presence of pigment in macrophages as evidence of hemorrhage due to violence. Other convincing proof, such as laceration of tissue in the proximity of such a tumor, is necessary.

DR. IRA COHEN: I wish to thank the discussers. The point made by Dr. Globus with reference to hemorrhage is well taken; in both cases there were gross clots, and in 1 this was so reported by Dr. Globus. I wish that Dr. Globus had differentiated more clearly—as he can do better than I—the difference between the so-called vascular malformations and the hemangiomas or angioblastic tumors, for I believe that in the cases reported here, as Dr. Globus said, the tumors were of true angioblastic type rather than malformations.

Recovery in Two Cases of Amyotrophic Lateral Sclerosis Treated with Tocopherol (Vitamin E). DR. I. S. WECHSLER.

I hesitated to present this material, first, because of my desire to make sure that my statements were correct and to verify the observations and, second, because of the nature of the disease. I wish to recall that amyotrophic lateral sclerosis is a fairly rapid, progressive, so-called degenerative disease of the nervous system,

without remissions, for which there is no satisfactory treatment. The disease almost invariably ends fatally within about two years, and most of the patients die of bulbar involvement. Before proceeding I shall give the reasons which prompted me to treat patients with tocopherol (an alcohol isolated from wheat germ oil, possessing the properties of vitamin E), and then tell of some of my experiences.

In the course of experiments on rats deprived of vitamin E for purposes of investigating sterility, carried out more than ten years ago, it was noted that atrophy developed in some animals. The atrophies occurred comparatively early and, once they appeared, persisted if not promptly treated. Most of the work was done on young rats. Goettsch and Pappenheim observed similar atrophies in rabbits. In 1936, Lipshutz reported on the neurologic findings in animals deprived of vitamin E (*Rev. neurol.* **65**:221 [Feb] 1936). Einarson and Ringsted (Effect of Chronic Vitamin E Deficiencies in the Nervous System and the Skeletal Musculature in Adult Rats, Copenhagen, Levin & Munksgaard, 1938) showed that there was degeneration of the posterior columns as well as of the anterior horn cells and the pyramidal tracts. In rats the pyramidal tract lies in the posterior column, not in the lateral, as it does in other animals. These authors drew an analogy between the degeneration of the pyramidal tracts and anterior horn cells and amyotrophic lateral sclerosis in man, and expressed the opinion that there must be a factor in vitamin E which is responsible for this degeneration. They did not know then, and I do not think it is known now, which factor causes the degeneration and which has to do with sterility.

On the basis of these facts, I decided to experiment with synthetic vitamin E in man, and last October I began to treat patients. From the description of animal experiments it seemed doubtful whether the degenerative process could be reversed after it was established and recovery be brought about. Perhaps only early in the course of the process could one reverse the degeneration. Unfortunately, one does not see cases of early amyotrophic lateral sclerosis. Patients either neglect their symptoms or are treated for a long time before the diagnosis is made; when they come to the neurologist they usually give a history of illness for from six to twelve months. By that time the signs of pyramidal lesions are fairly pronounced and the atrophies marked. In October I saw a patient whose history dated back only three months. Dr. Peter Denker had observed the patient and made the diagnosis. The man had atrophy of the left hand and of the interosseus muscles, fibrillations in the muscles of the arm and increased radial, ulnar, biceps, triceps and pectoral reflexes. He showed signs of involvement of the left pyramidal tract and some change in the abdominal reflexes. I made a diagnosis of amyotrophic lateral sclerosis, and sent the patient to Mount Sinai Hospital. The question of diagnosis was raised because of the rapid recovery. However, in the presence of atrophy and increased reflexes and the absence of sensory disturbance, I know of no other diagnosis one could make. The patient was thoroughly studied, including roentgenographic examination and studies of the spinal fluid, blood and electrical reactions. There was no history of previous inflammation, encephalitis or other disease.

The man had been receiving vitamin B, without effect. He was given ephynal, a synthetic vitamin E preparation. There is evidence to show that alpha tocopherol has to do with the degenerative process. The man received, in tablet form, tablets of tocopherol, of 3 mg. each, and promptly began to recover. Once he made an experiment on himself: For a few days he ran out of tocopherol, and the weakness began to return; he recovered when he received the vitamin E preparation again. When I first saw him he had wrist drop; he could not button his clothes or hold a knife or fork. After I began to treat him the fibrillations disappeared; the power returned, and the muscles began to fill in. After about six weeks of treatment I asked him whether he would care to make another experiment, and I stopped giving the tocopherol for four or five days; this time

he began to feel weak in the legs and hands. He promptly resumed the medication and has continued well until the time of this report.

The second patient, a woman aged 36, was admitted to Mount Sinai Hospital in August 1939. In October, a year previously, she had begun to have weakness in the arms and legs; the disease gradually developed until she had marked bulbar symptoms. She was bedridden and could not move her legs; she had difficulty in swallowing. On examination she gave a clearcut picture of amyotrophic lateral sclerosis—fibrillations and marked atrophy and fibrillation of the tongue, the "bag of worms" type. She had been taking vitamin B, and said she felt better. She also had been receiving better food, much of it containing vitamin E, but improvement was slight. After she was given a vitamin E preparation improvement became rapid, to the extent that the tongue lost its atrophy and the fibrillations disappeared. She got out of bed and was sent home, on her own feet. She can walk with assistance and can swallow with ease. The improvement was maintained until she acquired an acute respiratory infection, which set back her progress a little. Some of the fibrillations in the tongue recurred, but not the atrophy. Now that she has recovered from the acute respiratory infection, she feels much better.

I have treated a number of other patients. I gave them foodstuffs rich in vitamin E—namely, lettuce, other green vegetables, nuts, bread, beef fat and egg yolks. To saturate them with vitamin E, I subsequently added wheat germ oil in doses of 2 teaspoonfuls (8 cc.) daily. Fearing that there might be difficulty in absorption, I added tocopherol in oil intramuscularly, which was especially prepared for me. In view of the evidence adduced by Margulis and others that vitamin B_4, not vitamin B_1 or riboflavin and nicotinic acid, may have to do with the atrophies, I added the B complex, because vitamin B_4 is not available in crystalline form. One patient now in the hospital, a football player, who had the disease in an advanced form, has been treated for nine weeks. He has shown no progression of the disease, and the fibrillation has lessened. It is fair to say that the disease has been arrested in his case. Another patient, who has been treated for six weeks, has shown no progression. I must repeat that in both cases the disease was advanced. I am treating 6 patients at the Montefiore Hospital, all of them with advanced forms of the disease. In 3 cases the disease has been of such long duration that I wonder whether it is amyotrophic lateral sclerosis. Three others belong in this group, but it is too early to say whether the treatment is effective. One patient seen in consultation was treated for a week, but he was almost moribund when I saw him and died. Another patient, treated privately, with an advanced stage, has had the disease arrested.

I realize that it is too early to draw conclusions or to make any statement about ultimate cure. I think it is fair to say that 1 patient has shown complete recovery. Another patient, who according to all previous experience should have died by this time, has shown amazing partial recovery. I believe that tocopherol is responsible for the remarkable recovery. It may be that other factors entered into the treatment. My impression is that the gastrointestinal tract is involved in some way, and the history of 3 patients bears this out. One was treated for gallbladder disease for a year and was robbed of foodstuffs which contain vitamin E. I took meticulous histories of the diets of the patients for two or three years before the onset of their illness. Another patient was treated for a presumed gastric ulcer and lived on the Sippy diet. Still another patient, for a reason I do not know, had lived for the past six years on a diet which was particularly poor in vitamin E. When one compares the diet on which he lived with the diet which he is now receiving, one is struck by the enormous difference in the vitamin E content.

The question also arises whether some patients, though receiving enough vitamin E, fail to absorb it. Vitamin E is widely distributed in nature and there is no reason why people should be deprived of it, but it is known that otherwise adequate diets may be inadequate with regard to their vitamin content.

Whether the facts which I presented tonight will hold in other cases remains to be seen. It seems to me that another year at least will be necessary to determine their validity. I know it will be difficult to reverse advanced processes. My opinion is that the woman recovered from atrophy of the tongue because it was the most recent symptom and therefore was still reversible. The extremities have not recovered nearly so well. I think it is fair to say that one will be able to arrest even advanced processes, and so prevent fatalities. If, in the future, one can treat patients in the early stages it is probable that recoveries will be brought about.

There is an important theoretic point worth mentioning, namely, the light these experiments will throw on the word "degeneration." All know how meaningless the word is clinically. It is a pathologic description connoting the disappearance of myelin sheaths, axis-cylinders and nerve cells and their replacement with glial tissue. What degeneration is, how it is brought about, one does not know. The knowledge gained through experiments with vitamin B and the facts I have presented with regard to vitamin E may throw new light on the true meaning of "degeneration." One will then speak in terms of etiology and pathophysiology rather than of terminal pathology. This may point the way not only to better treatment, but also to better understanding of other so-called degenerative diseases.

DISCUSSION

DR. BERNARD SACHS: I congratulate Dr. Wechsler on this interesting paper. I shall not attempt to argue whether or not both the cases are true instances of amyotrophic lateral sclerosis. I dare say they are, but I think that is of less importance just now than other points they present. The results in these cases fit in remarkably with the success that is now being secured in the treatment of many muscular palsies and muscular dystrophies. In view of what has been done with regard to myasthenia, the immediate improvement in this and other conditions of muscular atrophy and paralysis that has been brought about, it is immaterial what label one gives to these disorders. I hope some day a cure will be available. It is important not to come to too hasty a conclusion regarding what the vitamins really accomplish in these cases. I am thoroughly impressed with their value, but I think one tends to be overawed by them. I am sure that Dr. Wechsler will agree that there may be other factors of as great or equal importance. This brings up a subject which it will be well to pursue carefully for some time, so that when conclusions are reached they will be definite and final.

DR. PETER G. DENKER: I am personally acquainted with the first patient whom Dr. Wechsler presented and have followed his progress under Dr. Wechsler's care with great interest. I can personally vouch for the marked improvement he has made. During the period of almost a week in which he abstained from tocopherol there was no question that he was rapidly slipping downhill. In the past few months, under treatment with the vitamin E extract, there has been return of muscle substance in his hands, so that the intrinsic atrophy is at present much less marked than previously. He has been able to return to business, take care of his affairs, walk about without fatigue and use his left hand almost as well as ever. However, I feel that there is a certain doubt as to the diagnosis. The onset of the illness was sudden, and the signs have always been confined to the left arm and left leg. He is something of a sailor, and it was while holding the wheel of his boat that he suddenly felt his left hand completely lose its power. There had been no trauma. He had always had an adequate diet, with no gastrointestinal symptoms that might explain a lack of vitamin absorption through diarrhea or vomiting. There was no history of venereal disease or anything resembling an episode of encephalitis, although it is known that encephalitis occasionally presents a clinical picture resembling that of amyotrophic lateral sclerosis. On examination, the findings have always been those of a lesion of the anterior horn cells and pyramidal tracts, with no sensory changes, which is

characteristic of this illness. I therefore agree with Dr. Wechsler that, though this is not a typical case of amyotrophic lateral sclerosis, it cannot be explained on any other basis. The important fact is that this man has unquestionably been greatly helped by tocopherol. Both subjectively and objectively this improvement has been striking, and I believe Dr. Wechsler is to be congratulated on this pioneering effort in the treatment of an illness which all have looked on as having a hopeless prognosis.

Dr. George H. Hyslop: I think Dr. Sachs is wrong in saying that terminology does not count. Dr. Sachs, if I understand him correctly, said he did not care what one calls this condition if one can cure it. One should not use the term "amyotrophic lateral sclerosis" as some use the phrase "multiple sclerosis"—loosely and to cover a number of clinical syndromes. Amyotrophic lateral sclerosis in all the textbooks has for some time been defined as a disease of the late middle period of life, with a gradual onset. The school of English workers has at times used the term amyotrophic lateral sclerosis for a syndrome which is spoken of in the United States as diffuse progressive muscular atrophy. They do not know why we Americans use the term amyotrophic lateral sclerosis as we do, and we cannot understand why they use it in the sense they do. The woman who was presented was not in the age group characteristic of the syndrome known as amyotrophic lateral sclerosis. The man had an abrupt onset of the illness. I do not question the importance of experimenting in any field of biochemistry which may give a better understanding of how to treat such patients. But I think one must still be careful actually to define what one means by a certain phrase. In using the term amyotrophic lateral sclerosis one should think of one thing, and not a medley of dissimilar disorders of the lower and upper motor neurons. I think that if one treated a man of 55 who had had a gradual onset of what is usually called amyotrophic lateral sclerosis with vitamin E, one would be disappointed in the results.

Dr. Israel Strauss: The first case described by Dr. Wechsler is one in which the diagnosis of amyotrophic lateral sclerosis might easily be questioned. First, the patient is young. Second, according to his physician's statement, made here tonight, the onset of the illness was acute.

Although there was no history of any previous infective process such as usually precedes the development of encephalomyeloradiculitis, the clinical picture might, nevertheless, be considered that of myeloradiculitis. The patient has improved greatly; yet he still has some atrophy of the muscles of the hand and some weakness and inability to use the hand with facility.

The second case, however, is one of great importance and significance. It is unquestionably a case of amyotrophic lateral sclerosis. Dr. Wechsler stated that there were marked atrophy and marked fibrillations of the tongue while the patient was under his observation. Tonight there is no such atrophy, and there are few fibrillations. In addition, the woman was bedridden and unable to walk. Tonight she was able to walk into the meeting with assistance. Furthermore, she suffered from dysphagia. Tonight she stated that she is able to eat everything and has no difficulty in swallowing. I have never in my experience with amyotrophic lateral sclerosis seen such improvement, and I do not recall a case in which there was recovery from bulbar symptoms.

Under the circumstances, one must consider carefully the results which Dr. Wechsler has presented. They cannot be dismissed as adventitious. One must admit that, whether owing to the administration of vitamin E in excess or to some method which has facilitated its absorption, an effect has been produced in the second case by this medication. Dr. Wechsler, furthermore, is conservative in his statement that a part of the process, particularly in the second case, must be recognized as irreversible.

The problem presented to the neurologist is that of being able to diagnose the disease in its early stages. If that can be done with any accuracy, one may find

that this method of treatment is of great value. I saw a patient of Dr. Wechsler's whom he had been treating with tocopherol. The disease was of bulbar type, and, interestingly, there were fibrillations involving the entire body, but no outstanding symptoms of the pyramidal tract. The man has not improved, and Dr. Wechsler does not know why he has not; but that does not militate against the possibility that this disease, which I am convinced is of endogenous origin, may have some connection with a deficiency in vitamins—whether of vitamin E alone or of others time alone can tell.

DR. NORMAN H. JOLLIFFE: Two points may have been overlooked. First, one must revise one's opinion of what constitutes an irreversible lesion. The second case which Dr. Wechsler presented emphasizes that point. Patients with lesions which heretofore have been considered irreversible, that experienced neurologists of long clinical experience have never before seen regress, make a recovery.

The second point is that when Dr. Wechsler presented his work on peripheral neuritis and the results of treatment with vitamin B in the winter of 1929 and 1930 and of 1932 and 1933, few believed him. Later work has proved the soundness of his conclusions at that time; future work will, I hope, substantiate his results in these 2 cases.

DR. TRACY J. PUTNAM: Dr. Wechsler has without question had two brilliant successes, and he must be congratulated on them. He is also to be congratulated on the caution and conservatism with which he has presented this subject. These 2 cases give food for thought concerning the treatment of amyotrophic lateral sclerosis. To me this comes as a considerable surprise, in view of the work of Einarson and Ringsted. The histologic picture which they demonstrated in rats as a result of lack of vitamin E seemed to me in many respects far removed from what is recognized as the typical histopathologic changes of amyotrophic lateral sclerosis. First, all their animals showed pronounced changes in the skin and sensory loss before they presented any evidence of loss of function of the pyramidal tracts. The evidence of loss of pyramidal function was never marked. The atrophy of the anterior horn cells was different from what one associates with amyotrophic lateral sclerosis. The authors pointed out that the disease looked more like a combination of combined system disease or tabes with amyotrophic lateral sclerosis than like amyotrophic lateral sclerosis itself. There are, of course, apparent transitions between these three conditions—the syphilitic amyotrophic lateral sclerosis, on the one hand, and the combined myelitis and lower motor neuron disease seen with deficiency diseases, on the other—but they must be considered as atypical.

Whether the disease which Dr. Wechsler has presented can be considered true amyotrophic lateral sclerosis, however, is not the chief consideration. His patients have done exceptionally well, but many more must be treated before one can know where one stands. However, I should like to see experimental avitaminosis produced in much larger animals than rats, which, after all, are rather distant cousins of man.

DR. ISRAEL WECHSLER: I am grateful for the criticism and some of the skepticism expressed. Indeed, I had certain misgivings of my own about the first patient; I shared the doubt with Dr. Denker and others of my colleagues; yet I do not know what other diagnosis to venture in view of the symptoms of which I spoke. If further proof were needed, I should point once more to the clinical experiment with exacerbation of symptoms on failure to take tocopherol and the prompt recovery on its readministration. I think this is fairly good evidence.

I wish to refer now to the work of Bicknell (*Lancet* **1**:10 [Jan. 6] 1940), which came to my attention in February, after the recovery occurred in the first 2 patients and after I had treated several others. Bicknell's work dealt essentially with the dystrophies, but he also reported 2 cases of recovery and 2 of death from amyotrophic lateral sclerosis. His work obviously confirms mine, as my work confirms his. I should add that, independently of Bicknell, I have been treating a patient with dystrophy, who is showing improvement.

As to the involvement of the posterior columns of Goll and Burdach, as shown by Einarson and Ringsted: Dr. Davidson and I reported cases of amyotrophic lateral sclerosis with disturbances of the posterior columns which were verified at autopsy. These are the only cases that I know of in which the anterior horn cells, the pyramidal tracts and the posterior columns were involved. We also reported cases in which other sensory disturbances and involvement of peripheral nerves complicated amyotrophic lateral sclerosis. While the classic picture is limited to the motor system, there may be isolated instances in which both the posterior columns and the peripheral system are affected.

With reference to the statement of Dr. Hyslop about spinal muscular atrophies, it is believed by some that they are one aspect of a process which, at the other end of the scale, includes amyotrophic lateral sclerosis. However, in the instances in which the disease is limited to the anterior horn cells or their nuclear homologues in the bulb, the syndrome is one of atrophies and loss of reflexes. This condition may have its onset at all ages and the patients live for ten or twenty years or longer. As to amyotrophic lateral sclerosis being a disease of old age, the statement will have to be revised. It is true that most of the cases occur after the age of 50, but many have seen undoubted cases of amyotrophic lateral sclerosis in patients much younger. I have seen it in the third, fourth and fifth decades of life.

I wish to emphasize that I have not used the word "cure." I can merely repeat as a fact that 2 patients improved remarkably and that several had arrest of the disease. I believe, if my observations are confirmed, that henceforth many fatalities may be prevented. That alone will be a contribution to the longevity of patients with amyotrophic lateral sclerosis, who generally die within a year or two after consulting the neurologist.

In answer to Dr. Putnam, I wish to say that I am working on monkeys, depriving them of vitamin E in order to be sure that one can reproduce the disease in animals closer to man than the lowly rat and the rabbit. If I succeed in producing atrophies, I shall treat one group and let the disease in another progress without treatment. Dr. Globus has said he will work on the pathology, that is, if enough pathologic changes are produced.

Spinal Epidural Infections: Surgical and Pathologic Considerations. Dr. E. Jefferson Browder and (by invitation) Dr. Russell Meyers, Brooklyn.

A series of 14 cases, 7 of which formed the basis of a previous communication, have been analyzed and the important clinical features tabulated. This report is limited to cases in which infection was established by metastatic invasion. In 12 instances vertebral osteomyelitis was proved to be present. The frequent observation of osteomyelitis and the symptoms of the clinical entity lend support to the opinion previously expressed that most spinal epidural infections of metastatic origin represent a complication of vertebral osteomyelitis. Autopsies were performed on 7 of the 8 patients of this series who died. The data so derived were supplemented by those obtained at operation in 9 cases. Study of the spinal cords and their membranes after removal indicated that compression of the cord was not the sole factor producing neurologic dysfunction. The changes suggested some type of local disturbance in the circulation (blood and/or cerebrospinal fluid) of the cord. Concerning this phenomenon no defensible theoretic explanation is available. In view of the time that usually elapses between the onset of the pain in the spine and the appearance of neurologic signs, a correct diagnosis should be arrived at and drainage by laminectomy instituted before the spinal cord has become implicated.

DISCUSSION

Dr. Harold R. Merwarth: Dr. Browder and Dr. Meyers deserve commendation for once more emphasizing osteomyelitis of the vertebrae as the essential causative factor in the production of an abscess of the spinal epidural space.

This contention, first proposed by the late Ramsay Hunt (*M. Rec.* **65**:641, 1904), had been ignored with few exceptions until the authors of this paper presented their first contribution on spinal epidural abscess (*Am. J. Surg.* **37**:4 [July] 1937).

The term spinal epidural abscess—acute and perhaps chronic—is sufficiently inclusive not to require further terminologic elaboration, which only beclouds the issue. Once the clinical concept of initial infectious involvement of the vertebral structure is thoroughly grasped, one clings to the descriptive simplicity embodied in this title to connote further extension into the epidural space.

Clinically, the disease is characteristic. Since it is most commonly embolic, there generally is elicited a history of infection elsewhere in the body. The pain, limited to a precise area of the spine, with resulting limitation of motion; the tenderness of the dorsal spinous process; the radicular qualities of the pain, and the clinical evidence of sepsis should always arouse suspicion of vertebral osteomyelitis. This early suspicion of infectious vertebral involvement is stressed, for without an intelligent concept of the course of events the significance of subsequent implication of the spinal cord may be altogether missed. It is a psychologic hurdle which must be jumped.

The diagnosis of spinal epidural abscess is established beyond doubt when clinical evidences of involvement of the spinal cord occur. In no situation is early surgical intervention more mandatory. Hesitating delay invites disaster. One even hopes that the stage may be reached at which a diagnosis of osteomyelitis of a vertebra can be made with confidence and certainty and the osteomyelitic abscess drained without awaiting the dangerous involvement of the cord as the indication for surgical intervention, or the development of terminal meningitis, which was noted twice in this series. The danger in awaiting signs of implication of the spinal cord for substantiation of a diagnosis was well illustrated in a case described tonight by Dr. Browder and Dr. Meyers in which there was no subarachnoid block and no evidence of compression of the spinal cord, and yet severe destructive changes were observed in the cord. This occurrence demonstrates clearly that if the abscess in the vertebra had been drained early the destructive changes in the cord would have been avoided.

The number of cases reported here indicates that spinal epidural abscess is not as rare as has been intimated. Direct invasion of the epidural space by an immediately adjacent infection occurs so infrequently that it tends to strengthen further the concept of primary vertebral osteomyelitis with secondary production of a spinal epidural abscess. It can be stated with considerable assurance that the picture of spinal epidural abscess is a definitely established clinical entity.

DR. IRA COHEN: The authors have presented in a clearcut manner a clinical entity which deserves more widespread recognition. It can be looked at from two aspects: one, the clinical, which is not in the least debatable, and the other, the pathologic, in which there are many points which are not entirely clear. In the majority of instances the short interval from the onset of severe pain in the back until the onset of neurologic signs cannot be too strongly emphasized. It is a matter usually of several days, sometimes as long as seven, occasionally longer, but usually between two and five days. It is at this time that the condition should be recognized and the patient operated on. In 1 case in this series the diagnosis was made within sixty-six hours of the time of onset of the pain and before there were any neurologic signs, other than meningeal and root irritation. If a patient can be operated on at that stage complete return of function may be had, provided the case does not fall into a second group, in which epidural infection is part of general sepsis. Then, regardless of the fact that the epidural space is drained, the sepsis may continue, with fatal outcome, unless the patient responds to chemotherapy. There is, however, a group of patients in which in a brief time, twenty-four or, at the most, forty-eight hours, after the onset of the pain there develops suddenly complete flaccid paraplegia, which is an irreversible process so far as is known. The patient's life may be saved, but the paralysis remains.

As to the pathologic picture, Dr. Browder and I have differed and still differ as to whether the process always starts in a vertebra. I have operated on patients in whom, as he has described, pus is seen in the soft tissues of the back and the spinous process of the vertebra may stand out like a sore thumb, bathed in pus. Undoubtedly, in such a case, and in many others, the process starts in the vertebra; I still believe, however, that there is a certain number of cases in which the infection starts in the epidural fat. The chronic granulomas support this point of view.

As to the nature of the process in the spinal cord, one is again on debatable ground. That compression alone has a great deal to do with the clinical picture cannot be denied, because it has been observed that a patient will present an ascending level from day to day, that is, a patient who has not the picture of a complete transverse lesion. On the other hand, pressure alone cannot explain the sudden onset, seen in many cases, of complete flaccid paraplegia.

It is well to bring even before a society such as this the importance of recognizing this condition, because it is only when it is diagnosed early that something can be accomplished.

Dr. Frank Fremont-Smith: I wish to emphasize a point that Dr. Cohen brought out, namely, the meningeal symptoms, which may occur early. Severe pain, headache and slight stiffness of the neck are characteristic of some of the acute forms, and may suggest tuberculous meningitis, particularly since the spinal fluid may show a picture identical with that in tuberculous meningitis, i. e., sugar at the low normal level, or even diminished, a predominantly lymphocytic reaction and high protein content. On the other hand, there is subarachnoid block, which is unusual in early tuberculous meningitis, while the high leukocyte count of the blood leads one to think of pyogenic infection. In the case which the authors mentioned in which operation was performed by Dr. R. Frank Slaughter at the neurologic unit of the Boston City Hospital, the patient, a girl of 16, was seen within two days of the onset of pain. She still had the healing scar of a furuncle on her temple, and the diagnosis was suspected from the clinical picture: pain, headache, slight stiffness of the neck, slight fever, severe pain in the back and the recently healed furuncle. There were no neurologic signs, except a slightly positive Kernig sign on the right and the pain. The diagnosis was confirmed at lumbar puncture, which revealed complete block and yellow fluid, containing 200 leukocytes (mostly polymorphonuclear), 420 mg. of protein, 58 mg. of sugar and 649 mg. of chlorides, per hundred cubic centimeters. Operation was performed five days after the onset, before any signs of compression of the cord had appeared, and the patient made a complete recovery (Slaughter, R. F.; Fremont-Smith, F., and Munro, D.: Metastatic Spinal Epidural Abscess, *J. A. M. A.* **102**:1468 [May 5] 1934).

Dr. Irving H. Pardee: Dr. Browder and Dr. Merwarth mentioned briefly the question of chemotherapy. Today there are available various preparations of sulfanilamide which are undoubtedly useful in cases of this type. I appreciate that with extensive osteomyelitis the problem is more difficult, but the response in the nervous system to these preparations is remarkable. Many patients with formerly incurable disease, such as meningitis, recover with the use of these preparations. Recently, a patient with an early unformed abscess of the brain, whom I have been watching carefully, has recovered, the cell count of the spinal fluid having fallen from 250 cells per cubic millimeter to normal, and the protein from 175 mg. per hundred cubic centimeter to normal, with the use of sulfapyridine. I think that under these circumstances if surgeons consider medicinal therapy first, provided the case is not an emergency, and then make use of a preparation of sulfanilamide after operation as well, the prognosis may be better than the results in this series would indicate.

Dr. E. D. Friedman: I wish to call attention to one or two facts which stand out in the pathologic slides which have been shown. First, in one of the pathologic

specimens there seemed to be degeneration chiefly in the lateral and posterior columns, an expression perhaps of a reaction to mild ischemia of the cord, manifested first in the phylogenetically newer structures. Second, more complete lesions of the cord are probably due to actual thrombosis and more complete occlusion of the vessels, so that the patient presents the clinical picture of transverse myelitis.

I was also interested in the finding of a clear spinal fluid, without increase in protein or manometric block, in a case in which the lesion was high in the cervical zone. That might be explained by the fact that the suboccipital space is very large; there is room, therefore, for accumulation of considerable exudate or for a neoplasm without resulting manometric block. It seems, then, that whatever signs of involvement of the cord are present are due not to pressure of the exudate on the cord itself, but to ischemia of the cord from the pressure exerted on the vessels by the inflammatory lesion.

Dr. E. Jefferson Browder: I wish to thank the several discussers. I cannot enter into a controversy with Dr. Cohen regarding the pathogenesis of this particular lesion. There are instances in which one cannot demonstrate osteomyelitis. On the other hand, we have had a case of granuloma in which roentgen examination disclosed a definite lesion of the body of the vertebra.

Dr. Friedman spoke of a case that was used as an illustration in the paper in which the lesion was located in the cervical region. The osteomyelitic process was at the level of the fifth cervical vertebra, and the implication of the spinal cord extended over approximately six segments. It seems possible that the changes in the spinal cord may be explained on the basis of the venous alterations, as Dr. Friedman outlined.

Dr. Pardee spoke of chemotherapy. We have now under observation, I think, an undoubted instance of spinal epidural infection in which occur all the classic features of this disease. Sulfamethylthiazole is being given, and there have been recession in the paretic state of the lower extremities and improvement in the toxemia, which frequently accompanies this disorder out of all proportion to the degree of fever.

Note.—Sulfamethylthiazole is no longer on the market.

Focal Cerebral Ischemia and Reactive Gliosis Following Experimental Vascular Spasm. Dr. Francis A. Echlin (by invitation).

By means of photographs and photomicrographs it has been shown that the pial arterial vessels in the cat will constrict on mechanical or electrical (thyratron) stimulation. Florey, in 1925, was the first to demonstrate this fact adequately. It has been found that the pial vessels of the dog are not as sensitive to this form of stimulation as those of the cat, and those of the monkey are less so than those of the dog.

Evidence is presented which strongly indicates that stretch of a pial vessel is an adequate stimulus to produce contraction of the smooth muscle and constriction of the vessel wall. This suggests that the tone of a pial blood vessel, at least in the cat, may be partly maintained by a purely local mechanism, i. e., intra-arterial pressure (or stretch).

It is shown (by use of a thermoelectric blood flow recorder) that diminished blood flow in the cortex can be produced by constricting the pial vessels with mechanical or electrical stimulation.

This fact is also demonstrated by intravital staining. A photograph is shown of a cat's brain into which gentian violet was injected by way of the femoral vein while the vessels over the suprasylvian gyrus were being stimulated electrically with the thyratron. The gyrus stimulated remained white, while the remainder of the brain became blue. The same fact is demonstrated by the injection of chlorazol sky blue.

Coronal sections of these brains show that the ischemia is frequently in the form of a triangular zone in the gray matter.

It is thought that the triangular shape of the ischemic patches is undoubtedly explained by the anatomic distribution of the perforating arterial vessels from the pia in each gyrus. If only a few neighboring vessels are completely constricted over the surface of a gyrus, the ischemic patch will be in the form of a small triangle corresponding to the distribution of these vessels. At times, of course, the ischemia will be patchy, first, because the constrictions may be patchy and, second, because of the unevenness of the supply of collateral blood vessels.

Since ischemia occurs in this manner, one may expect to see pathologic lesions in the cortex corresponding to such triangular areas of ischemia after electrical stimulation. This is shown to be true in cats that have been allowed to survive two or more weeks after ischemia was produced in the cortex by the aforementioned method. A thyratron was used for stimulation, and the strength of the stimulus employed was usually just sufficient to produce movement when applied to the motor cortex.

Anatomically, the lesions occur in the form of a large, or a smaller, triangular zone of gliosis in the gray matter, or are perivascular and patchy. The lesions are mainly evidenced by hypertrophy and increase in the number of astrocytes, but in the more severe lesions changes in nerve cells, and even complete disorganization and destruction of the normal cytoarchitecture in the triangular area are observed. It has been demonstrated that the lesion can be varied from one of patchy nature to a small or large triangular area of marked pathologic change by varying the intensity and duration of the electrical stimulation, i. e., the degree and duration of the ischemia.

In a number of cats in which the brains were merely exposed to air for two hours at operation and which were then allowed to survive for two or more weeks, lesions are found anatomically and histologically similar to those observed in the cats' brains after electrical stimulation. These lesions are presumably also due to ischemia of the gray matter, but how this is produced and how consistent this particular change will prove to be remain to be shown by further study. In these lesions the hypertrophied astrocytes tend to be more evenly distributed throughout the triangular zone, and the gliosis is less patchy than in the lesions following electrical stimulation.

Further discussion of the theoretic application of the facts reported will be postponed until the work is published in detail.

DISCUSSION

DR. LEWIS STEVENSON: The preparations made by Dr. Echlin with Cajal's gold chloride-mercury bichloride method are much more convincing than the photographs, because one can see the entire patch of gliosis. The explanation of the gliosis is unknown to me. It is something new. I am accustomed to think of gliosis as occurring when nerve cells are lost; the microglia eat them up, and then the astrocytes lay down a scar. In these preparations there is little reaction on the part of the microglia, and little need for it, because few of the nerve cells are destroyed, except in the cases of severe electrical stimulation. This gliosis is interesting, because it occurs with simple exposure of the brain as well as with electrical stimulation; perhaps those who are occustomed to expose a brain for from six to twelve hours and stimulate it may be glad to know that this may be not without serious effect on the patient's nervous system.

DR. E. JEFFERSON BROWDER: Dr. Echlin has reported important observations, which are somewhat disturbing to surgeons. I wish to ask if any observations have been made under conditions such as exist at operation. Certainly, one does not expose the brain to a drying process for two hours. One should be meticulous about keeping covered all areas of the exposed brain not under consideration at any given time.

DR. FRANCIS A. ECHLIN: In my presentation there was an observation which I failed to mention; I wish to do so now. In a number of cats which had recovered

from ether anesthesia, focal cerebral ischemia or ischemia of a large portion of a hemisphere was produced by electrical stimulation of the pial vessels. These cats did not have epileptic seizures, or movements of any kind, so long as stimulation was not carried forward to the motor gyrus. This, of course, does not prove that subclinical epileptiform neuronal discharges did not take place as a result of the ischemia.

As far as the last part of my presentation is concerned, I do not wish to be too definite concerning the effect on the brain of exposing it to air. I wish to study a much larger series of animals to determine whether the observations presented on this aspect of the problem will prove to be consistent.

Dr. Browder asked about drying. A number of the cats had the brain irrigated with Ringer's solution at body temperature, for two hours, during the period of exposure; these animals also showed at the end of two to three weeks a triangular patch of gliosis in the gray matter. This triangular patch varied; it was not always marked. Sometimes there was only slight hypertrophy of the astrocytes, but it was found whether the cortex was kept dry or wet.

Book Reviews

The Physiology and Pharmacology of the Pituitary Body. Volume II. By H. B. Van Dyke. Price, $4.50. Pp. 401, with 10 tables and 29 illustrations. Chicago: University of Chicago Press, 1939.

In 1936, Van Dyke published a book reviewing the literature on the physiology of the hypophysis up to the beginning of 1935. The present volume supplements this by discussing the papers published between 1935 and the beginning of 1938. In spite of this short interval, more than 1,400 titles are mentioned in the bibliography. The presentation of this enormous material is clear and concise and never tiresome to read. The neurologist will be interested particularly in the author's discussion of the relation of the hypothalamus to the pituitary gland. The recent work on the autonomic innervation of the pituitary is carefully evaluated. An exhaustive index increases the value of the book for purposes of reference. Altogether, it is a masterly piece of work.